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<p>(21) International Application Number: PCT/US99/05028</p> <p>(22) International Filing Date: 8 March 1999 (08.03.99)</p> <p>(30) Priority Data:</p> <table border="0"> <tr> <td>60/077,450</td> <td>10 March 1998 (10.03.98)</td> <td>US</td> </tr> <tr> <td>60/077,632</td> <td>11 March 1998 (11.03.98)</td> <td>US</td> </tr> <tr> <td>60/077,641</td> <td>11 March 1998 (11.03.98)</td> <td>US</td> </tr> </table> <p><i>(Continued on the following page)</i></p> <p>(71) Applicant (for all designated States except US): GENENTECH, INC. [US/US]; One DNA Way, South San Francisco, CA 94080 (US).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): WOOD, William, I. [US/US]; 35 South Down Court, Hillsborough, CA 94010 (US). GODDARD, Audrey [CA/US]; 110 Congo Street, San Francisco, CA 94131 (US). GURNEY, Austin [US/US]; 1 Debbie Lane, Belmont, CA 94002 (US). YUAN, Jean [CN/US]; 176 West 37th Avenue, San Mateo, CA 94403 (US). BAKER, Kevin, P. [GB/US]; 1115 South Grant Street, San Mateo, CA 94402 (US). CHEN, Jian [CN/US]; 1860 Ogden Drive #4, Burlingame, CA 94010 (US).</p> <p>(74) Agents: KRESNAK, Mark, T. et al.; Genentech Inc., 1 DNA Way, South San Francisco CA 94080-4990 (US).</p>	60/077,450	10 March 1998 (10.03.98)	US	60/077,632	11 March 1998 (11.03.98)	US	60/077,641	11 March 1998 (11.03.98)	US	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b></p> <p><i>Without international search report and to be republished upon receipt of that report.</i></p>
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(54) Title: NOVEL POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME										
<p>(57) Abstract</p> <p>The present invention is directed to novel polypeptides and nucleic acids encoding said polypeptides. Also provided herein are vectors and host cells comprising those nucleic acid sequences, chimeric polypeptide molecules comprising the polypeptides of the present invention fused to heterologous polypeptide sequences, antibodies which bind to the polypeptides of the present invention and to methods for producing the polypeptides of the present invention.</p>										

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(30) 60/080,165	31 Mar/mar 1998 (31.03.1998)	US	(30) 60/083,495	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/086,414	22 May/mal 1998 (22.05.1998)	US
(30) 60/080,194	31 Mar/mar 1998 (31.03.1998)	US	(30) 60/083,558	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/086,392	22 May/mal 1998 (22.05.1998)	US
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(30) 60/080,333	1 Apr/avr 1998 (01.04.1998)	US	(30) 60/083,559	29 Apr/avr 1998 (29.04.1998)	US	(30) 60/087,208	28 May/mal 1998 (28.05.1998)	US
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(30) 60/080,334	1 Apr/avr 1998 (01.04.1998)	US	(30) 60/083,742	30 Apr/avr 1998 (30.04.1998)	US	(30) 60/087,106	28 May/mal 1998 (28.05.1998)	US
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## NOVEL POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME

### FIELD OF THE INVENTION

The present invention relates generally to the identification and isolation of novel DNA and to the recombinant production of novel polypeptides encoded by that DNA.

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### BACKGROUND OF THE INVENTION

Extracellular proteins play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

15 Secreted proteins have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

20 Membrane-bound proteins and receptors can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process,

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can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. Efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

We herein describe the identification and characterization of novel secreted and transmembrane polypeptides and novel nucleic acids encoding those polypeptides.

#### 1. PRO213

Human growth arrest-specific gene 6 (gas6) encodes a protein that is expressed in a variety of different tissues and which has been reported to be highly expressed during periods of serum starvation and negatively regulated during growth induction. See Manfioletti et al., *Mol. Cell. Biol.* 13(8):4976-4985 (1993) and Stitt et al., *Cell* 80:661-670 (1995). Manfioletti et al. (1993), *supra*, have suggested that the gas6 protein is member of the vitamin K-dependent family of proteins, wherein the members of the latter family of proteins (which include, for example, Protein S, Protein C and Factor X) all play regulatory roles in the blood coagulation pathway. Thus, it has been suggested that gas6 may play a role in the regulation of a protease cascade relevant in growth regulation or in the blood coagulation cascade.

Given the physiological importance of the gas6 protein, efforts are currently being undertaken by both industry and academia to identify new, native proteins which are homologous to gas6. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins, specifically those having homology to gas6. Examples of such screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe the identification of a novel polypeptide which has homology to the gas6 polypeptide.

#### 2. PRO274

The 7-transmembrane ("7TM") proteins or receptors, also referred to in the literature as G-protein coupled receptors, are specialized proteins designed for recognition of ligands and the subsequent signal transduction of information contained within those ligands to the machinery of the cell. The primary purpose of cell surface receptors is to discriminate appropriate ligands from the various extracellular stimuli which each cell encounters, then to activate an effector system that produces an intracellular signal, thereby controlling cellular processes. [Dohlman, H., *Ann. Rev. Biochem.*, 60:653 (1991)]. The ability of 7TM receptors to bind ligand to a recognition domain and allosterically transmit the information to an intracellular domain is a



specialized feature of 7TM proteins [Kenakin, T., Pharmacol. Rev., 48:413 (1996)]. The gene family which encodes the 7TM receptors or G-protein linked receptors encode receptors which recognize a large number of ligands, including but not limited to, C5a, interleukin 8 and related chemokines. Research in this area suggests that distinct signals at the cell surface feed into common pathways of cell activation. [Gerard, C. and Gerard, N., Curr. Op. Immunol., 6:140 (1994), Gerard, C. and Gerard, N., Ann. Rev. Immunol., 12:775 (1994)]. The superfamily of 7TM or G-protein coupled receptors contains several hundred members able to recognize various messages such as photons, ions and amino acids among others [Schwartz, T.W., et al., H., Trends in Pharmacol. Sci., 17(6):213 (1996)]. [Dohlman, H., Ann. Rev. Biochem., 60:653 (1991)]. [Schwartz, T.W., et al., H., Eur. J. Pharm. Sci., 2:85 (1994)]. We describe herein the identification of a novel polypeptide (designated herein as PRO274) which has homology to the 7 transmembrane segment receptor proteins and the Fn54 protein.

### 3. PRO300

The Diff 33 protein is over-expressed in mouse testicular tumors. At present its role is unclear, however, it may play a role in cancer. Given the medical importance of understanding the physiology of cancer, efforts are currently being under taken to identify new, native proteins which are involved in cancer. We describe herein the identification of a novel polypeptide which has homology to Diff 33, designated herein as PRO300.

### 4. PRO284

Efforts are currently being undertaken to identify and characterize novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide, designated herein as PRO284.

### 5. PRO296

Cancerous cells often express numerous proteins that are not expressed in the corresponding normal cell type or are expressed at different levels than in the corresponding normal cell type. Many of these proteins are involved in inducing the transformation from a normal cell to a cancerous cell or in maintaining the cancer phenotype. As such, there is significant interest in identifying and characterizing proteins that are expressed in cancerous cells. We herein describe the identification and characterization of a novel polypeptide having homology to the sarcoma-amplified protein SAS, designated herein as PRO296.

### 6. PRO329

Immunoglobulin molecules play roles in many important mammalian physiological processes. The structure of immunoglobulin molecules has been extensively studied and it has been well documented that intact immunoglobulins possess distinct domains, one of which is the constant domain or F<sub>c</sub> region of the immunoglobulin molecule. The F<sub>c</sub> domain of an immunoglobulin, while not being directly involved in antigen

recognition and binding, does mediate the ability of the immunoglobulin molecule, either uncomplexed or complexed with its respective antigen, to bind to F<sub>c</sub> receptors either circulating in the serum or on the surface of cells. The ability of an F<sub>c</sub> domain of an immunoglobulin to bind to an F<sub>c</sub> receptor molecule results in a variety of important activities, including for example, in mounting an immune response against unwanted foreign particles. As such, there is substantial interest in identifying novel F<sub>c</sub> receptor proteins and subunits thereof.

5 We herein describe the identification and characterization of a novel polypeptide having homology to a high affinity immunoglobulin F<sub>c</sub> receptor protein, designated herein as PRO329.

#### 7. PRO362

Colorectal carcinoma is a malignant neoplastic disease which has a high incidence in the Western world, particularly in the United States. Tumors of this type often metastasize through lymphatic and vascular channels and result in the death of some 62,000 persons in the United States annually.

Monoclonal antibody A33 (mAbA33) is a murine immunoglobulin that has undergone extensive preclinical analysis and localization studies in patients inflicted with colorectal carcinoma (Welt et al., *J. Clin. Oncol.* 8:1894-1906 (1990) and Welt et al., *J. Clin. Oncol.* 12:1561-1571 (1994)). mAbA33 has been shown to bind to an antigen found in and on the surface of normal colon cells and colon cancer cells. In carcinomas originating from the colonic mucosa, the A33 antigen is expressed homogeneously in more than 95% of the cases. The A33 antigen, however, has not been detected in a wide range of other normal tissues, i.e., its expression appears to be rather organ specific. Therefore, the A33 antigen appears to play an important role in the induction of colorectal cancer.

Given the obvious importance of the A33 antigen in tumor cell formation and/or proliferation, there is substantial interest in identifying homologs of the A33 antigen. In this regard, we herein describe the identification and characterization of a novel polypeptide having homology to the A33 antigen protein, designated herein as PRO362.

#### 8. PRO363

The cell surface protein HCAR is a membrane-bound protein that acts as a receptor for subgroup C of the adenoviruses and subgroup B of the coxsackieviruses. Thus, HCAR may provide a means for mediating viral infection of cells in that the presence of the HCAR receptor on the cellular surface provides a binding site for viral particles, thereby facilitating viral infection.

In light of the physiological importance of membrane-bound proteins and specifically those which serve as a cell surface receptor for viruses, efforts are currently being undertaken by both industry and academia to identify new, native membrane-bound receptor proteins. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. We herein describe a novel membrane-bound polypeptide having homology to the cell surface protein HCAR and to various tumor antigens including A33 and carcinoembryonic antigen, designated herein as PRO363, wherein this

polypeptide may be a novel cell surface virus receptor or tumor antigen.

#### 9. PRO868

Control of cell numbers in mammals is believed to be determined, in part, by a balance between cell proliferation and cell death. One form of cell death, sometimes referred to as necrotic cell death, is typically characterized as a pathologic form of cell death resulting from some trauma or cellular injury. In contrast, there is another, "physiologic" form of cell death which usually proceeds in an orderly or controlled manner. This orderly or controlled form of cell death is often referred to as "apoptosis" [see, e.g., Barr et al., Bio/Technology, 12:487-493 (1994); Steller et al., Science, 267:1445-1449 (1995)]. Apoptotic cell death naturally occurs in many physiological processes, including embryonic development and clonal selection in the immune system [Itoh et al., Cell, 66:233-243 (1991)]. Decreased levels of apoptotic cell death have been associated with a variety of pathological conditions, including cancer, lupus, and herpes virus infection [Thompson, Science, 267:1456-1462 (1995)]. Increased levels of apoptotic cell death may be associated with a variety of other pathological conditions, including AIDS, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis, retinitis pigmentosa, cerebellar degeneration, aplastic anemia, myocardial infarction, stroke, reperfusion injury, and toxin-induced liver disease [see, Thompson, supra].

Apoptotic cell death is typically accompanied by one or more characteristic morphological and biochemical changes in cells, such as condensation of cytoplasm, loss of plasma membrane microvilli, segmentation of the nucleus, degradation of chromosomal DNA or loss of mitochondrial function. A variety of extrinsic and intrinsic signals are believed to trigger or induce such morphological and biochemical cellular changes [Raff, Nature, 356:397-400 (1992); Steller, supra; Sachs et al., Blood, 82:15 (1993)]. For instance, they can be triggered by hormonal stimuli, such as glucocorticoid hormones for immature thymocytes, as well as withdrawal of certain growth factors [Watanabe-Fukunaga et al., Nature, 356:314-317 (1992)]. Also, some identified oncogenes such as *myc*, *rel*, and *E1A*, and tumor suppressors, like *p53*, have been reported to have a role in inducing apoptosis. Certain chemotherapy drugs and some forms of radiation have likewise been observed to have apoptosis-inducing activity [Thompson, supra].

Various molecules, such as tumor necrosis factor- $\alpha$  ("TNF- $\alpha$ "), tumor necrosis factor- $\beta$  ("TNF- $\beta$ " or "lymphotoxin- $\alpha$ "), lymphotoxin- $\beta$  ("LT- $\beta$ "), CD30 ligand, CD27 ligand, CD40 ligand, OX-40 ligand, 4-1BB ligand, Apo-1 ligand (also referred to as Fas ligand or CD95 ligand), and Apo-2 ligand (also referred to as TRAIL) have been identified as members of the tumor necrosis factor ("TNF") family of cytokines [See, e.g., Gruss and Dower, Blood, 85:3378-3404 (1995); Pitti et al., J. Biol. Chem., 271:12687-12690 (1996); Wiley et al., Immunity, 3:673-682 (1995); Browning et al., Cell, 72:847-856 (1993); Armitage et al. Nature, 357:80-82 (1992), WO 97/01633 published January 16, 1997; WO 97/25428 published July 17, 1997]. Among these molecules, TNF- $\alpha$ , TNF- $\beta$ , CD30 ligand, 4-1BB ligand, Apo-1 ligand, and Apo-2 ligand (TRAIL) have been reported to be involved in apoptotic cell death. Both TNF- $\alpha$  and TNF- $\beta$  have been reported to induce apoptotic death in susceptible tumor cells [Schmid et al., Proc. Natl. Acad. Sci., 83:1881 (1986); Dealtry et al., Eur. J.

Immunol., 17:689 (1987)]. Zheng et al. have reported that TNF- $\alpha$  is involved in post-stimulation apoptosis of CD8-positive T cells [Zheng et al., Nature, 377:348-351 (1995)]. Other investigators have reported that CD30 ligand may be involved in deletion of self-reactive T cells in the thymus [Amakawa et al., Cold Spring Harbor Laboratory Symposium on Programmed Cell Death, Abstr. No. 10, (1995)].

5 Mutations in the mouse Fas/Apo-1 receptor or ligand genes (called *lpr* and *gld*, respectively) have been associated with some autoimmune disorders, indicating that Apo-1 ligand may play a role in regulating the clonal deletion of self-reactive lymphocytes in the periphery [Krammer et al., Curr. Op. Immunol., 6:279-289 (1994); Nagata et al., Science, 267:1449-1456 (1995)]. Apo-1 ligand is also reported to induce post-stimulation apoptosis in CD4-positive T lymphocytes and in B lymphocytes, and may be involved in the elimination of activated lymphocytes when their function is no longer needed [Krammer et al., supra; Nagata et al., supra].

10 Agonist mouse monoclonal antibodies specifically binding to the Apo-1 receptor have been reported to exhibit cell killing activity that is comparable to or similar to that of TNF- $\alpha$  [Yonehara et al., J. Exp. Med., 169:1747-1756 (1989)].

Induction of various cellular responses mediated by such TNF family cytokines is believed to be initiated by their binding to specific cell receptors. Two distinct TNF receptors of approximately 55-kDa (TNFR1) and 75-kDa (TNFR2) have been identified [Hohman et al., J. Biol. Chem., 264:14927-14934 (1989); Brockhaus et al., Proc. Natl. Acad. Sci., 87:3127-3131 (1990); EP 417,563, published March 20, 1991] and human and mouse cDNAs corresponding to both receptor types have been isolated and characterized [Loetscher et al., Cell, 61:351 (1990); Schall et al., Cell, 61:361 (1990); Smith et al., Science, 248:1019-1023 (1990); Lewis et al., Proc. Natl. Acad. Sci., 88:2830-2834 (1991); Goodwin et al., Mol. Cell. Biol., 11:3020-3026 (1991)].

20 Extensive polymorphisms have been associated with both TNF receptor genes [see, e.g., Takao et al., Immunogenetics, 37:199-203 (1993)]. Both TNFRs share the typical structure of cell surface receptors including extracellular, transmembrane and intracellular regions. The extracellular portion of both receptors are found naturally also as soluble TNF-binding proteins [Nophar, Y. et al., EMBO J., 9:3269 (1990); and Kohno, T. et al., Proc. Natl. Acad. Sci. U.S.A., 87:8331 (1990)]. More recently, the cloning of recombinant soluble TNF

25 receptors was reported by Hale et al. [J. Cell. Biochem. Supplement 15F, 1991, p. 113 (P424)].

The extracellular portion of type 1 and type 2 TNFRs (TNFR1 and TNFR2) contains a repetitive amino acid sequence pattern of four cysteine-rich domains (CRDs) designated 1 through 4, starting from the NH<sub>2</sub>-terminus. Each CRD is about 40 amino acids long and contains 4 to 6 cysteine residues at positions which are well conserved [Schall et al., supra; Loetscher et al., supra; Smith et al., supra; Nophar et al., supra; Kohno et al., supra]. In TNFR1, the approximate boundaries of the four CRDs are as follows: CRD1- amino acids 14 to about 53; CRD2- amino acids from about 54 to about 97; CRD3- amino acids from about 98 to about 138; CRD4- amino acids from about 139 to about 167. In TNFR2, CRD1 includes amino acids 17 to about 54; CRD2- amino acids from about 55 to about 97; CRD3- amino acids from about 98 to about 140; and CRD4- amino acids from about 141 to about 179 [Banner et al., Cell, 73:431-435 (1993)]. The potential role of the

30 CRDs in ligand binding is also described by Banner et al., supra.

A similar repetitive pattern of CRDs exists in several other cell-surface proteins, including the p75 nerve

growth factor receptor (NGFR) [Johnson et al., *Cell*, 47:545 (1986); Radeke et al., *Nature*, 325:593 (1987)], the B cell antigen CD40 [Stamenkovic et al., *EMBO J.*, 8:1403 (1989)], the T cell antigen OX40 [Mallet et al., *EMBO J.*, 9:1063 (1990)] and the Fas antigen [Yonehara et al., *supra* and Itoh et al., *Cell*, 66:233-243 (1991)]. CRDs are also found in the soluble TNFR (sTNFR)-like T2 proteins of the Shope and myxoma poxviruses [Upton et al., *Virology*, 160:20-29 (1987); Smith et al., *Biochem. Biophys. Res. Commun.*, 176:335 (1991); Upton et al., *Virology*, 184:370 (1991)]. Optimal alignment of these sequences indicates that the positions of the cysteine residues are well conserved. These receptors are sometimes collectively referred to as members of the TNF/NGF receptor superfamily. Recent studies on p75NGFR showed that the deletion of CRD1 [Welcher, A.A. et al., *Proc. Natl. Acad. Sci. USA*, 88:159-163 (1991)] or a 5-amino acid insertion in this domain [Yan, H. and Chao, M.V., *J. Biol. Chem.*, 266:12099-12104 (1991)] had little or no effect on NGF binding [Yan, H. and Chao, M.V., *supra*]. p75 NGFR contains a proline-rich stretch of about 60 amino acids, between its CRD4 and transmembrane region, which is not involved in NGF binding [Peetre, C. et al., *Eur. J. Hematol.*, 41:414-419 (1988); Seckinger, P. et al., *J. Biol. Chem.*, 264:11966-11973 (1989); Yan, H. and Chao, M.V., *supra*]. A similar proline-rich region is found in TNFR2 but not in TNFR1.

The TNF family ligands identified to date, with the exception of lymphotoxin- $\alpha$ , are type II transmembrane proteins, whose C-terminus is extracellular. In contrast, most receptors in the TNF receptor (TNFR) family identified to date are type I transmembrane proteins. In both the TNF ligand and receptor families, however, homology identified between family members has been found mainly in the extracellular domain ("ECD"). Several of the TNF family cytokines, including TNF- $\alpha$ , Apo-1 ligand and CD40 ligand, are cleaved proteolytically at the cell surface; the resulting protein in each case typically forms a homotrimeric molecule that functions as a soluble cytokine. TNF receptor family proteins are also usually cleaved proteolytically to release soluble receptor ECDs that can function as inhibitors of the cognate cytokines.

Recently, other members of the TNFR family have been identified. Such newly identified members of the TNFR family include CAR1, HVEM and osteoprotegerin (OPG) [Brojatsch et al., *Cell*, 87:845-855 (1996); Montgomery et al., *Cell*, 87:427-436 (1996); Marsters et al., *J. Biol. Chem.*, 272:14029-14032 (1997); Simonet et al., *Cell*, 89:309-319 (1997)]. Unlike other known TNFR-like molecules, Simonet et al., *supra*, report that OPG contains no hydrophobic transmembrane-spanning sequence.

Moreover, a new member of the TNF/NGF receptor family has been identified in mouse, a receptor referred to as "GITR" for "glucocorticoid-induced tumor necrosis factor receptor family-related gene" [Nocentini et al., *Proc. Natl. Acad. Sci. USA* 94:6216-6221 (1997)]. The mouse GITR receptor is a 228 amino acid type I transmembrane protein that is expressed in normal mouse T lymphocytes from thymus, spleen and lymph nodes. Expression of the mouse GITR receptor was induced in T lymphocytes upon activation with anti-CD3 antibodies, Con A or phorbol 12-myristate 13-acetate. It was speculated by the authors that the mouse GITR receptor was involved in the regulation of T cell receptor-mediated cell death.

In Marsters et al., *Curr. Biol.*, 6:750 (1996), investigators describe a full length native sequence human polypeptide, called Apo-3, which exhibits similarity to the TNFR family in its extracellular cysteine-rich repeats and resembles TNFR1 and CD95 in that it contains a cytoplasmic death domain sequence [see also Marsters et

al., Curr. Biol., 6:1669 (1996)]. Apo-3 has also been referred to by other investigators as DR3, wsl-1 and TRAMP [Chinnaiyan et al., Science, 274:990 (1996); Kitson et al., Nature, 384:372 (1996); Bodmer et al., Immunity, 6:79 (1997)].

Pan et al. have disclosed another TNF receptor family member referred to as "DR4" [Pan et al., Science, 276:111-113 (1997)]. The DR4 was reported to contain a cytoplasmic death domain capable of engaging the cell suicide apparatus. Pan et al. disclose that DR4 is believed to be a receptor for the ligand known as Apo-2 ligand or TRAIL.

In Sheridan et al., Science, 277:818-821 (1997) and Pan et al., Science, 277:815-818 (1997), another molecule believed to be a receptor for the Apo-2 ligand (TRAIL) is described. That molecule is referred to as DR5 (it has also been alternatively referred to as Apo-2). Like DR4, DR5 is reported to contain a cytoplasmic death domain and be capable of signaling apoptosis.

In Sheridan et al., supra, a receptor called DcR1 (or alternatively, Apo-2DcR) is disclosed as being a potential decoy receptor for Apo-2 ligand (TRAIL). Sheridan et al. report that DcR1 can inhibit Apo-2 ligand function *in vitro*. See also, Pan et al., supra, for disclosure on the decoy receptor referred to as TRID.

For a review of the TNF family of cytokines and their receptors, see Gruss and Dower, supra.

As presently understood, the cell death program contains at least three important elements - activators, inhibitors, and effectors; in *C. elegans*, these elements are encoded respectively by three genes, *Ced-4*, *Ced-9* and *Ced-3* [Steller, Science, 267:1445 (1995); Chinnaiyan et al., Science, 275:1122-1126 (1997); Wang et al., Cell, 90:1-20 (1997)]. Two of the TNFR family members, TNFR1 and Fas/Apo1 (CD95), can activate apoptotic cell death [Chinnaiyan and Dixit, Current Biology, 6:555-562 (1996); Fraser and Evan, Cell, 85:781-784 (1996)]. TNFR1 is also known to mediate activation of the transcription factor, NF- $\kappa$ B [Tartaglia et al., Cell, 74:845-853 (1993); Hsu et al., Cell, 84:299-308 (1996)]. In addition to some ECD homology, these two receptors share homology in their intracellular domain (ICD) in an oligomerization interface known as the death domain [Tartaglia et al., supra; Nagata, Cell, 88:355 (1997)]. Death domains are also found in several metazoan proteins that regulate apoptosis, namely, the *Drosophila* protein, Reaper, and the mammalian proteins referred to as FADD/MORT1, TRADD, and RIP [Cleaveland and Ihle, Cell, 81:479-482 (1995)].

Upon ligand binding and receptor clustering, TNFR1 and CD95 are believed to recruit FADD into a death-inducing signalling complex. CD95 purportedly binds FADD directly, while TNFR1 binds FADD indirectly via TRADD [Chinnaiyan et al., Cell, 81:505-512 (1995); Boldin et al., J. Biol. Chem., 270:387-391 (1995); Hsu et al., supra; Chinnaiyan et al., J. Biol. Chem., 271:4961-4965 (1996)]. It has been reported that FADD serves as an adaptor protein which recruits the *Ced-3*-related protease, MACH $\alpha$ /FLICE (caspase 8), into the death signalling complex [Boldin et al., Cell, 85:803-815 (1996); Muzio et al., Cell, 85:817-827 (1996)]. MACH $\alpha$ /FLICE appears to be the trigger that sets off a cascade of apoptotic proteases, including the interleukin-1 $\beta$  converting enzyme (ICE) and CPP32/Yama, which may execute some critical aspects of the cell death programme [Fraser and Evan, supra].

It was recently disclosed that programmed cell death involves the activity of members of a family of cysteine proteases related to the *C. elegans* cell death gene, *ced-3*, and to the mammalian IL-1-converting

enzyme, ICE. The activity of the ICE and CPP32/Yama proteases can be inhibited by the product of the cowpox virus gene, *crmA* [Ray et al., *Cell*, 69:597-604 (1992); Tewari et al., *Cell*, 81:801-809 (1995)]. Recent studies show that CrmA can inhibit TNFR1- and CD95-induced cell death [Enari et al., *Nature*, 375:78-81 (1995); Tewari et al., *J. Biol. Chem.*, 270:3255-3260 (1995)].

As reviewed recently by Tewari et al., TNFR1, TNFR2 and CD40 modulate the expression of proinflammatory and costimulatory cytokines, cytokine receptors, and cell adhesion molecules through activation of the transcription factor, NF- $\kappa$ B [Tewari et al., *Curr. Op. Genet. Develop.*, 6:39-44 (1996)]. NF- $\kappa$ B is the prototype of a family of dimeric transcription factors whose subunits contain conserved Rel regions [Verma et al., *Genes Develop.*, 9:2723-2735 (1996); Baldwin, *Ann. Rev. Immunol.*, 14:649-681 (1996)]. In its latent form, NF- $\kappa$ B is complexed with members of the I $\kappa$ B inhibitor family; upon inactivation of the I $\kappa$ B in response to certain stimuli, released NF- $\kappa$ B translocates to the nucleus where it binds to specific DNA sequences and activates gene transcription.

#### 10. PRO382

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized, including the serine proteases which exhibit specific activity toward various serine-containing proteins. The mammalian protease enzymes play important roles in biological processes such as, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

In light of the important physiological roles played by protease enzymes, efforts are currently being undertaken by both industry and academia to identify new, native protease homologs. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe the identification of novel polypeptides having homology to serine protease enzymes, designated herein as PRO382 polypeptides.

#### 11. PRO545

The ADAM (A Disintegrin And Metalloprotease) family of proteins of which meltrin is a member may have an important role in cell interactions and in modulating cellular responses. [see, for example, Gilpin et al., *J. Biol. Chem.*, 273(1):157-166 (1998)]. The ADAM proteins have been implicated in carcinogenesis. Meltrin- $\alpha$  (ADAM12) is a myoblast gene product reported to be required for cell fusion. [Harris et al., *J. Cell. Biochem.*, 67(1):136-142 (1997), Yagami-Hiromasa et al., *Nature*, 377:652-656 (1995)]. The meltrins contain disintegrin and metalloprotease domains and are implicated in cell adhesive events involved in development, through the integrin-binding disintegrin domain, but also have an anti-adhesive function through a zinc-dependent metalloprotease domain. [Alfandari et al., *Devel. Biol.*, 182(2):314-330 (1997)]. Given the medical importance

of cell fusion and modulation of cellular responses in carcinogenesis and other disease mechanisms, efforts are currently being under taken to identify new, native proteins which are involved in cell fusion and modulation of cellular responses. We describe herein the identification of a novel polypeptide which has homology to meltrin, designated herein as PRO545.

5    12.    PRO617

CD24 is a protein that is associated with the cell surface of a variety of different cells of the mammalian immune system, including for example, neutrophils, monocytes and some lymphocytes, for example, B lymphocytes. CD24 has been shown to be a ligand for the platelet-associated surface glycoprotein P-selectin (also known as granule membrane protein-140 or GMP-140), a glycoprotein that is constitutively synthesized  
10 in both platelets and endothelial cells and becomes exposed on the surface of platelets when those cells become activated. In this way, P-selectin mediates the calcium-dependent adhesion of activated platelets and endothelial cells to the various cells of the immune system that express one or more ligands for the P-selectin molecule, particularly CD24. This mechanism allows for recruitment of immune system cells to locations where they are most needed, for example, sites of injury. Thus, there is substantial interest in identifying novel polypeptides  
15 that exhibit homology to the cell surface antigens of the immune system cells. We herein describe the identification and characterization of a novel polypeptide having homology to the CD24 protein, wherein that novel polypeptide is herein designated PRO617.

13.    PRO700

20    Protein-disulfide isomerase (PDI) is a catalyst of disulfide formation and isomerization during protein folding. It has two catalytic sites housed in two domains homologous to thioredoxin, one near the N terminus and the other near the C terminus. [See, for example, Gilbert HF, *J. Biol. Chem.*, 272:6969-6972 (1997), Mayfield KJ, *Science*, 278:1954-1957 (1997) and Puig et al., *J. Biol. Chem.*, 272:32988-32994 (1997)]. PDI is useful for formation of natural type disulfide bonds in a protein which is produced in a prokaryotic cell. (See  
25 also, U.S. Patent Nos. 5,700,659 and 5,700,678).

Thus, PDI and molecules related thereto are of interest, particularly for ability to catalyze the formation of disulfide bonds. Moreover, these molecules are generally of interest in the study of redox reactions and related processes. PDI and related molecules are further described in Darby, et al., *Biochemistry* 34, 11725-11735 (1995). We herein describe the identification and characterization of novel polypeptides having homology  
30 to protein disulfide isomerase, designated herein as PRO700 polypeptides.

14.    PRO702

Conglutinin is a bovine serum protein that was originally described as a vertebrate lectin protein and which belongs to the family of C-type lectins that have four characteristic domains, (1) an N-terminal cysteine-rich domain, (2) a collagen-like domain, (3) a neck domain and (4) a carbohydrate recognition domain (CRD).  
35 Recent reports have demonstrated that bovine conglutinin can inhibit hemagglutination by influenza A viruses



as a result of their lectin properties (Eda et al., Biochem. J. 316:43-48 (1996)). It has also been suggested that lectins such as conglutinin can function as immunoglobulin-independent defense molecules due to complement-mediated mechanisms. Thus, conglutinin has been shown to be useful for purifying immune complexes *in vitro* and for removing circulating immune complexes from patients plasma *in vivo* (Lim et al., Biochem. Biophys. Res. Commun. 218:260-266 (1996)). We herein describe the identification and characterization of a novel polypeptide having homology to the conglutinin protein, designated herein as PRO702.

15. PRO703

Very-long-chain acyl-CoA synthetase ("VLCAS") is a long-chain fatty acid transport protein which is active in the cellular transport of long and very long chain fatty acids. [see for example, Uchida et al., J Biochem (Tokyo) 119(3):565-571 (1996) and Uchiyama et al., J Biol Chem 271(48):30360-30365 (1996)]. Given the biological importance of fatty acid transport mechanisms, efforts are currently being under taken to identify new, native proteins which are involved in fatty acid transport. We describe herein the identification of a novel polypeptide which has homology to VLCAS, designated herein as PRO703.

15 16. PRO705

The glypicans are a family of glycosylphosphatidylinositol (GPI)-anchored proteoglycans that, by virtue of their cell surface localization and possession of heparin sulfate chains, may regulate the responses of cells to numerous heparin-binding growth factors, cell adhesion molecules and extracellular matrix components. Mutations in one glypican protein cause of syndrome of human birth defects, suggesting that the glypicans may play an important role in development (Litwack et al., Dev. Dyn. 211:72-87 (1998)). Also, since the glypicans may interact with the various extracellular matrices, they may also play important roles in wound healing (McGrath et al., Pathol. 183:251-252 (1997)). Furthermore, since glypicans are expressed in neurons and glioma cells, they may also play an important role in the regulation of cell division and survival of cells of the nervous system (Liang et al., J. Cell. Biol. 139:851-864 (1997)). It is evident, therefore, that the glypicans are an extremely important family of proteoglycans. There is, therefore, substantial interest in identifying novel polypeptides having homology to members of the glypican family. We herein describe the identification and characterization of a novel polypeptide having homology to K-glypican, designated herein as PRO705.

17. PRO708

30 Aryl sulfatases are enzymes that exist in a number of different isoforms, including aryl sulfatase A (ASA), aryl sulfatase B (ASB) and aryl sulfatase C (ASC), and that function to hydrolyze a variety of different aromatic sulfates. Aryl sulfatases have been isolated from a variety of different animal tissues and microbial sources and their structures and functions have been extensively studied (see, e.g., Nichol and Roy, J. Biochem. 55:643-651 (1964)). ASA deficiency has been reported to be associated with metachromatic leukodystrophy (MLD) (Giles et al., Prenat. Diagn. 7(4):245-252 (1987) and Herska et al., Am. J. Med. Genet. 26(3):629-635 (1987)). Additionally, other groups have reported that aryl sulfatases have been found in high levels in natural

killer cells of the immune system and have hypothesized a possible role for these enzymes in NK cell-mediated cellular lysis (see, e.g., Zucker-Franklin et al., Proc. Natl. Acad. Sci. USA 80(22):6977-6981 (1983)). Given the obvious physiological importance of the aryl sulfatase enzymes, there is a substantial interest in identifying novel aryl sulfatase homolog polypeptides. We herein describe the identification and characterization of novel polypeptides having homology to the aryl sulfatases, wherein these novel polypeptides are herein designated

5 PRO708 polypeptides.

#### 18. PRO320

Fibulin-1 is a cysteine-rich, calcium-binding extracellular matrix (ECM) component of basement membranes and connective tissue elastic fibers and plasma protein, which has four isoforms, A-D, derived from alternative splicing. Fibulin-1 is a modular glycoprotein with amino-terminal anaphylatoxin-like modules followed by nine epidermal growth factor (EGF)-like modules and, depending on alternative splicing, four possible carboxyl termini. Fibulin-2 is a novel extracellular matrix protein frequently found in close association with microfibrils containing either fibronectin or fibrillin. There are multiple forms of fibulin-1 that differ in their C-terminal regions that are produced through the process of alternative splicing of their precursor RNA. [see

10 for example Tran et al., Matrix Biol 15(7):479-493 (1997).]

Northern and Western blotting analysis of 16 cell lines established from tumors formed in athymic mice and malignant cell lines derived from patients indicate that low expression of fibulin-1D plays a role in tumor formation and invasion. [Qing et al., Oncogene, 18:2159-2168 (1997)]. Ovarian-cancer cells are characterized by their ability to invade freely the peritoneal cavity. It has been demonstrated that estradiol stimulates the proliferation of estrogen-receptor (ER)-positive ovarian-cancer cells, as well as expression of fibulin-1. Studies on the effect of fibulin-1 on motility of the MDA-MB231 breast-cancer cell line, indicated inhibition of haptotactic migration of MDA-MB231 cells, and the authors concluded that fibulin-1 can inhibit cancer cell motility *in vitro* and therefore has the potential to inhibit tumor invasion. [Hayashido et al., Int J Cancer, 75(4):654-658 (1998)]

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Thus, fibulin, and molecules related thereto are of interest, particularly for the use of preventing cancer. Moreover, these molecules are generally of interest in the study of connective tissue and attachment molecules and related mechanisms. Fibulin and related molecules are further described in Adams, et al., J. Mol. Biol., 272(2):226-36 (1997); Kielty and Shuttleworth, Microsc. Res. Tech., 38(4):413-27 (1997); and Child, J. Card. Surg., 12(2Supp.):131-5 (1997).

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We herein describe the identification and characterization of novel polypeptides having homology to fibulin, designated herein as PRO320 polypeptides.

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#### 19. PRO324

Oxidoreductases are enzymes that catalyze a reaction in which two molecules of a compound interact so that one molecule is oxidized and the other is reduced, with a molecule of water entering the reaction. There are many different types of oxidoreductase enzymes that play very important physiological roles in the

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mammalian organism. Some of the most important oxidoreductases include, for example, lyases, lactases, cholesterol oxidases, and the like. These enzymes play roles in such essential processes as digestion, signal transduction, maintenance of ionic homeostasis, and the like. As such, given that oxidoreductase enzymes find various essential uses in the mammalian organism, there is a substantial interest in identifying novel oxidoreductase enzyme homologs. We herein describe the identification and characterization of a novel polypeptide having homology to oxidoreductases, designated herein as PRO324.

## 20. PRO351

Prostasin is a novel human serine proteinase purified from human seminal fluid. Immunohistochemical localization reveals that prostasin is present in epithelial cells and ducts of the prostate gland. The cDNA for prostasin has been cloned and characterized. Southern blot analysis, following a reverse transcription polymerase chain reaction, indicates that prostasin mRNA is expressed in prostate, liver, salivary gland, kidney, lung, pancreas, colon, bronchus, renal proximal tubular cells, and prostate carcinoma LNCaP cells. Cellular localization of prostasin mRNA was identified within epithelial cells of the human prostate gland by in situ hybridization histochemistry. [See for example, Yu et al., *J Biol Chem.* (1994) 269(29):18843-18848, and Yu et al., *J Biol Chem.* (1994) 270(22):13483-13489].

Thus, prostasin, and molecules related thereto are of interest, particularly for the study, diagnosis and treatment of medical conditions involving the prostate. Prostasin and related molecules are further described in Yu et al., *Genomics* (1996) 32(3):334-340. We herein describe the identification and characterization of novel polypeptides having homology to prostasin, designated herein as PRO351 polypeptides.

## 21. PRO352

Butyrophilin is a milk glycoprotein that constitutes more than 40% of the total protein associated with the fat globule membrane in mammalian milk. Expression of butyrophilin mRNA has been shown to correlate with the onset of milk fat production toward the end pregnancy and is maintained throughout lactation. Butyrophilin has been identified in bovine, murine and human (see Taylor et al., *Biochim. Biophys. Acta* 1306:1-4 (1996), Ishii et al., *Biochim. Biophys. Acta* 1245:285-292 (1995), Mather et al., *J. Dairy Sci.* 76:3832-3850 (1993) and Banghart et al., *J. Biol. Chem.* 273:4171-4179 (1998)) and is a type I transmembrane protein that is incorporated into the fat globulin membrane. It has been suggested that butyrophilin may play a role as the principle scaffold for the assembly of a complex with xanthine dehydrogenase/oxidase and other proteins that function in the budding and release of milk-fat globules from the apical surface during lactation (Banghart et al., *supra*).

Given that butyrophilin plays an obviously important role in mammalian milk production, there is substantial interest in identifying novel butyrophilin homologs. We herein describe the identification and characterization of a novel polypeptide having homology to butyrophilin, designated herein as PRO352.

22. **PRO381**

The immunophilins are a family of proteins that function as receptors for immunosuppressant drugs, such as cyclosporin A, FK506, and rapamycin. The immunophilins occur in two separate classes, (1) the FK506-binding proteins (FKBPs), which bind to FK506 and rapamycin, and (2) the cyclophilins, which bind to cyclosporin A. With regard to the FK506-binding proteins, it has been reported that the FK506/FKBP complex functions to inhibit the activity of the serine/threonine protein phosphatase 2B (calcineurin), thereby providing immunosuppressant activity (Gold, *Mol. Neurobiol.* 15:285-306 (1997)). It has also been reported that the FKBP immunophilins are found in the mammalian nervous system and may be involved in axonal regeneration in the central nervous system through a mechanism that is independent of the process by which immunosuppression is achieved (Gold, *supra*). Thus, there is substantial interest in identifying novel polypeptides having homology to the FKBP immunophilins. We herein describe the identification and characterization of a novel polypeptide having homology to an FKBP immunophilin protein, designated herein as PRO381.

23. **PRO386**

Mammalian cell membranes perform very important functions relating to the structural integrity and activity of various cells and tissues. Of particular interest in membrane physiology is the study of transmembrane ion channels which act to directly control a variety of physiological, pharmacological and cellular processes. Numerous ion channels have been identified including calcium (Ca), sodium (Na) and potassium (K) channels, each of which have been analyzed in detail to determine their roles in physiological processes in vertebrate and insect cells.

One type of cell membrane-associated ion channel, the sodium channel, plays an extremely important role in a cell's ability to maintain ionic homeostasis as well as transmit intracellular and extracellular signals. Voltage-gated sodium channels in brain neurons have been shown to be complexes of a pore-forming alpha unit with smaller beta-1 and beta-2 subunits (Isom et al., *Cell* 83:433-442 (1995)). Given the obvious importance of sodium channels in cellular homeostasis and other important physiological functions, there is a significant interest in identifying novel polypeptides having homology to sodium channel subunits. We herein describe the identification and characterization of a novel polypeptide having homology to the beta-2 subunit of the rat sodium channel, designated herein as PRO386.

24. **PRO540**

Lecithin-cholesterolacyltransferase ("LCAT"), also known as phosphatidylcholine-sterol acyltransferase is a key enzyme in the intravascular metabolism of high density lipoproteins, specifically in the process of cholesterol metabolism. [see, for example, Brousseau et al., *J. Lipid Res.* 38(12):2537-2547 (1997), Hill et al., *Biochem. J.*, 294:879-884 (1993), and Drayna et al., *Nature* 327 (6123):632-634 (1987)]. Given the medical importance of lipid metabolism, efforts are currently being under taken to identify new, native proteins which are involved in lipid transport. We describe herein the identification of a novel polypeptide which has homology

to LCAT, designated herein as PRO540.

25. **PRO615**

Synaptogyrin is a synaptic vesicle protein that is uniformly distributed in the nervous system. The cDNA encoding synaptogyrin has been cloned and sequenced and the sequence predicts a protein with a molecular mass of 25,900 D with four membrane-spanning domains. Synaptogyrin has been implicated in membrane traffic to and from the plasma membrane. Stenius et al., *J. Cell. Biol.* 131(6-2):1801-1809 (1995). In addition, a novel isoform of synaptogyrin called cellugyrin exhibits sequence identity with synaptogyrin. In rat tissues, cellugyrin and synaptogyrins are expressed in mirror image patterns. Cellugyrin is ubiquitously present in all tissues tested with the lowest levels in brain tissue, whereas synaptogyrin protein is only detectable in brain. In rat tissues, cellugyrin and synaptogyrins are expressed in mirror image patterns. The synaptic vesicle protein synaptogyrin may be a specialized version of a ubiquitous protein, cellugyrin, with the two proteins sharing structural similarity but differing in localization. This finding supports the emerging concept of synaptic vesicles as the simplified and specialized form of a generic trafficking organelle. [Janz et al., *J. Biol. Chem.* 273(5):2851-2857 (1998)] . The sequence for cellugyrin derived from the Norway rat, *Rattus norvegicus* has been deposited in the Genbank database on 23 December 1997, designated accession number AF039085. See also, Janz et al., *J. Biol. Chem.* 273 (1998), in press.

Given the medical importance of synaptic transmission, efforts are currently being under taken to identify new, native proteins that may be part of a simplified and specialized generic trafficking organelle in the form of synaptic vesicles. We describe herein the identification of a novel polypeptide which has homology to synaptogyrin, designated herein as PRO615.

26. **PRO618**

Enteropeptidase is a key enzyme in the intestinal digestion cascade specifically cleaves the acidic propeptide from trypsinogen to yield active trypsin. This cleavage initiates a cascade of proteolytic reactions leading to the activation of many pancreatic zymogens.

See, for example, Matsushima et al., *J. Biol. Chem.* 269(31):19976-19982 (1994), Kitamoto et al., *Proc. Nat. Acad. Sci.*, 91(16):7588-7592 (1994). Enterokinase (enteropeptidase) is related to mammalian serine proteases involved in digestion, coagulation, and fibrinolysis. LaVallie et al., *J Biol Chem.*, 268(31):23311-23317 (1993).

Given the medical importance of digestive processes, efforts are currently being under taken to identify new, native proteins that may be involved in digestion, coagulation, and fibrinolysis. We describe herein the identification of a novel polypeptide which has homology to enteropeptidase, designated herein as PRO618.

27. **PRO719**

Lipoprotein lipase is a key enzyme that mediates the hydrolysis of triglycerides and phospholipids present in circulating plasma lipoproteins (Dugi et al., *J. Biol. Chem.*, 270:25396-25401 (1995)). Moreover, lipoprotein lipase has been shown to mediate the uptake of lipoproteins into cells, wherein cellular uptake of

lipoproteins is initiated by binding of lipoprotein lipase to cell surface proteoglycans and to the low density lipoprotein (LDL) receptor-related protein (Krapp et al., J. Lipid Res. 36:2362-2373 (1995)). Thus, it is clear that lipoprotein lipase plays an extremely important role in lipoprotein and cholesterol metabolism. There is, therefore, substantial interest in identifying novel polypeptides that share sequence homology and/or biological activity with lipoprotein lipase. We herein describe the identification and characterization of a novel polypeptide having sequence homology to lipoprotein lipase H, designated herein as PRO719.

## 28. PRO724

The low density lipoprotein (LDL) receptor is a membrane-bound protein that plays a key role in cholesterol homeostasis, mediating cellular uptake of lipoprotein particles by high affinity binding to its ligands, apolipoprotein (apo) B-100 and apoE. The ligand-binding domain of the LDL receptor contains 7 cysteine-rich repeats of approximately 40 amino acids, wherein each repeat contains 6 cysteines, which form 3 intra-repeat disulfide bonds. These unique structural features provide the LDL receptor with its ability to specifically interact with apo B-100 and apoE, thereby allowing for transport of these lipoprotein particles across cellular membranes and metabolism of their components. Soluble fragments containing the extracellular domain of the LDL receptor have been shown to retain the ability to interact with its specific lipoprotein ligands (Simmons et al., J. Biol. Chem. 272:25531-25536 (1997)). Thus, it is clear that the LDL receptor is intimately involved in important physiological activities related to cholesterol metabolism. As such, there is substantial interest in identifying novel LDL receptor homolog proteins. We herein describe the identification and characterization of a novel polypeptide having homology to the human LDL receptor protein, designated herein as PRO724..

## 29. PRO772

Expression of the human gene A4 is enriched in the colonic epithelium and is transcriptionally activated on differentiation of colonic epithelial cells in vitro (Oliva et al., Arch. Biochem. Biophys. 302:183-192 (1993) and Oliva et al., Am. J. Physiol. 272:C957-C965 (1997)). A4 cDNA contains an open reading frame that predicts a polypeptide of approximately 17 kilodaltons in size. Hydropathy analysis of the A4 protein revealed four putative membrane-spanning alpha-helices. Immunocytochemical studies of cells expressing A4 protein indicated that expression is localized to the endoplasmic reticulum. The four membrane-spanning domains and the biophysical characteristics of the A4 protein suggest that it belongs to a family of integral membrane proteins called proteolipids, some of which multimerize to form ion channels. In fact, preliminary evidence has suggested that A4 may itself multimerize and take on the properties of an ion channel (Oliva et al., Am. J. Physiol. 272:C957-C965 (1997)). Given the importance of ion channels in maintaining cellular homeostasis, there is a significant interest in identifying novel polypeptides having homology to known and putative ion channels. We herein describe the identification and characterization of a novel polypeptide having homology to the putative ion channel protein, A4, designated herein as PRO772.

**30.     PRO852**

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized. The mammalian protease enzymes play important roles in many different biological processes including, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

In light of the important physiological roles played by protease enzymes, efforts are currently being undertaken by both industry and academia to identify new, native protease homologs. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe the identification of novel polypeptides having homology to various protease enzymes, designated herein as PRO852 polypeptides.

**31.     PRO853**

Studies have reported that the redox state of the cell is an important determinant of the fate of the cell. Furthermore, reactive oxygen species have been reported to be cytotoxic, causing inflammatory disease, including tissue necrosis, organ failure, atherosclerosis, infertility, birth defects, premature aging, mutations and malignancy. Thus, the control of oxidation and reduction is important for a number of reasons, including control and prevention of strokes, heart attacks, oxidative stress, hypertension and may be associated with the development of malignancies. The levels of antioxidant enzymes, such as reductases, which catalyze the conversion of reactive oxygen species to water have been shown to be low in cancer cells. In particular, malignant prostate epithelium may have lowered expression of such antioxidant enzymes [Baker et al., Prostate 32(4):229-233 (1997)]. In this regard, reductases, are of interest. In addition, the transcription factors, NF-kappa B and AP-1, are known to be regulated by redox state and to affect the expression of a large variety of genes thought to be involved in the pathogenesis of AIDS, cancer, atherosclerosis and diabetic complications. Publications further describing this subject matter include Engman et al., Anticancer Res. (Greece), 17:4599-4605 (1997), Kelsey, et al., Br. J. Cancer, 76(7):852-4 (1997); Friedrich and Weiss, J. Theor. Biol., 187(4):529-40 (1997) and Pieulle, et al., J. Bacteriol., 179(18):5684-92 (1997). Given the physiological importance of redox reactions *in vivo*, efforts are currently being under taken to identify new, native proteins which are involved in redox reactions. We describe herein the identification of a novel prostate specific polypeptide which has sequence similarity to reductase, designated herein as PRO853.

**32.     PRO860**

Neurofascin is a member of the L1 subgroup of the cellular adhesion molecule ("CAM") family of nervous system adhesion molecules and is involved in cellular aggregation. Cell-cell recognition and patterning

of cell contacts have a critical role in mediating reversible assembly of a wide variety of transcellular complexes in the nervous system. Cell interactions may be regulated through modulation of ankyrin binding to neurofascin. See, for example, Tuvia et al., Proc. Nat. Acad. Sci., 94(24) 12957-12962 (1997). Neurofascin has been described as a member of the L1 subgroup of the immunoglobulin superfamily implicated in neurite extension during embryonic development for which numerous isoforms have been detected at various stages of development. See also Hassel et al., J. Biol. Chem., 272(45) 28742-28749 (1997), Grumet., Cell. Tissue Res. 290(2) 423-428 (1997), Garver et al., J. Cell. Biol., 137:703-714 (1997), and Lambert et al., J. Neurosci., 17:7025-7-36 (1997),.

Given the physiological importance of cellular adhesion molecules and development of the nervous system *in vivo*, efforts are currently being under taken to identify new, native proteins which are involved in regulation of cellular interactions in the nervous system. We describe herein the identification and characterization of a novel polypeptide which has sequence similarity to neurofascin, designated herein as PRO860.

### 33. PRO846

The CMRF35 monoclonal antibody was used to identify a cell membrane antigen, designated CMRF35, which is present on the surface of monocytes, neutrophils, a proportion of peripheral blood T and B lymphocytes and lymphocytic cell lines. The CMRF35 cDNA encodes a novel integral membrane glycoprotein member of the immunoglobulin (Ig) gene superfamily. The molecule comprises (a) a single extracellular Ig variable domain remarkably similar to the Fc receptor for polymeric IgA and IgM, (b) a membrane-proximal domain containing a high proportion of proline, serine and threonine residues that was predicted to be heavily O-glycosylated, (c) an unusual transmembrane anchor that contained a glutamic acid and a proline residue and (d) a short cytoplasmic tail. Transcripts encoding the CMRF35 protein have been detected in early monocytic cell lines, in peripheral blood T cells and in some B lymphoblastoid cell lines, confirming the results of immunocytological staining. Jackson et al., Eur. J. Immunol. 22(5):1157-1163 (1992). CMRF-35 molecules are differentially expressed in hematopoietic cells, and the expression of the antigen was shown to be markedly influenced by stimulation with mitogens and cytokines. See, for example, Clark et al., Exp. Hematol. 25(8):759 (1997), Daish et al., Immunol. 79(1):55-63 (1993), and Clark et al., Tissue Antigens 48:461 (1996).

Given the physiological importance of the immune system and antigens associated with various immune system cells, efforts are currently being under taken to identify new, native proteins which are expressed on various cells of the immune system. We describe herein the identification of a novel polypeptide which has sequence similarity to CMRF35, designated herein as PRO846.

### 34. PRO862

Lysozyme is a protein which is widely distributed in several human tissues and secretions including milk, tears and saliva. It has been demonstrated to hydrolyze linkages between N-acetylglucosamines. It has been demonstrated to be an inhibitor of chemotaxis and of the production of toxic oxygen free radicals and may also



have some role in the calcification process. As such, there is substantial interest in identifying novel polypeptides having homology to lysozyme. We describe herein the identification of a novel polypeptide which has sequence similarity to lysozyme.

35. **PRO864**

5 Wnt-4 is a secreted glycoprotein which correlates with, and is required for, kidney tubulogenesis. Mice lacking Wnt-4 activity fail to form pretubular cell aggregates; however, other aspects of mesenchymal and ureteric development are unaffected. Thus, Wnt-4 appears to act as an autoinducer of the mesenchyme to epithelial transition that underlies nephron development. Stark et al., Nature ;372(6507):679-683 (1994). In addition, members of the Wnt gene family code for cysteine-rich, secreted proteins, which are differentially  
10 expressed in the developing brain and possibly act as intercellular signaling molecules. A Wnt gene, e.g., Wnt-1 is known to be essential for specification of the midbrain cell fate. Yoshioka et al., Biochem. Biophys. Res. Commun. 203(3):1581-1588 (1994). Several member of the Wnt family of secreted factors are strongly implicated as regulators of mammary cellular growth and differentiation. Shimizu et al., Cell Growth Differ. 8(12) 1349-1358. Wnt-4 is normally expressed in early pregnancy. Wnt-4 may therefore be a local signal  
15 driving epithelial branching in pregnancy. Edwards PA, Biochem Soc Symp. 63:21-34 (1998). See also, Lipschutz JH, Am. J. Kidney Dis. 31(3):383-397, (1998). We describe herein the identification and characterizaton of a novel polypeptide which has sequence similarity to Wnt-4, designated herein as PRO864.

36. **PRO792**

20 At least two cell-derived signals have been shown to be necessary for the induction of immunoglobulin isotype switching in B-cells. The first signal is given by either of the soluble lymphokines, interleukin (IL)-4 or IL-13, which induce germline epsilon transcript expression, but this alone is insufficient to trigger expression of immunoglobulin E (IgE). The second signal is provided by a physical interaction between B-cells and activated T-cells, basophils and mast cells, and it has been shown that the CD40/CD40 ligand pairing is crucial  
25 for mediating IgE synthesis. Additionally, amongst the numerous pairs of surface adhesion molecules that are involved in IgE synthesis, the CD23/CD21 pair appears to play a key role in the generation of IgE. CD23 is a protein that is positively and negatively regulated by factors which increase or decrease IgE production, respectively. Antibodies to CD23 have been shown to inhibit IL-4-induced human IgE production *in vitro* and to inhibit antigen-specific IgE responses in a rat model, in an isotype selective manner (Bonney et al., Eur.  
30 Respir. J. Suppl. 22:63S-66S (1996)). CD23 interacts with CD21 on B-cells, preferentially driving IgE production. Given that the CD23 protein plays an extremely important role in the induction of a mammalian IgE response, there is significant interest in identifying novel polypeptides having homology to CD23. We herein describe the identification and characterization of a novel polypeptide having homology to CD23, designated herein as PRO792.

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37. PRO866

Mindin and spondin proteins are secreted proteins that are structurally related to one another and which have been identified in a variety of organisms. For example, Higashijima et al., Dev Biol. 192:211-227 (1997) have reported the identification of spondin and mindin expression in floor plate cells in the zebrafish embryonic axis, thereby suggesting that mindin and spondin proteins play important roles in embryonic development. This same group has reported that mindin and spondin proteins function as extracellular matrix proteins that have a high affinity for the basal lamina. (Id.). It has been reported that F-spondin is a secreted protein that promotes neural adhesion and neurite extension (Klar et al., Cell 69:95-110 (1992) and that M-spondin is an extracellular matrix protein that localizes to muscle attachment sites in Drosophila (Umekiya et al., Dev. Biol. 186:165-176 (1997)). Thus, there is significant interest in identifying novel polypeptides having homology to the mindin and spondin proteins. We herein describe the identification and characterization of a novel polypeptide having homology to mindin2 and mindin1, designated herein as PRO866.

38. PRO871

Cyclophilins are a family of proteins that bind to cyclosporin A and possess peptidyl-prolyl cis-trans isomerase activity (Sherry et al., Proc. Natl. Acad. Sci. USA 95:1758-1763 (1998)). In addition, cyclophilins are secreted by activated cells and act in a cytokine-like manner, presumably via signaling through a cell surface cyclophilin receptor. Host cell-derived cyclophilin A has been shown to be incorporated into HIV-1 virions and its incorporation has been shown to be essential for viral infectivity. Thus, one or more of the cyclophilins may be directly associated with HIV-1 infectivity. Given the obvious importance of the cyclophilin proteins, there is substantial interest in identifying novel polypeptides which have sequence homology to one or more of the cyclophilin proteins. We herein describe the identification and characterization of a novel polypeptide having homology to cyclophilin-like protein Cyp-60, designated herein as PRO871.

39. PRO873

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Enzymes have also been shown to play important roles in combating various diseases and disorders. For example, liver carboxylesterases have been reported to assist in sensitizing human tumor cells to the cancer prodrugs. Danks et al., report that stable expression of the cDNA encoding a carboxylesterase in Rh30 human rhabdomyosarcoma cells increased the sensitivity of the cells to the CPT-11 cancer prodrug 8.1-fold. Cancer Res. (1998) 58(1):20-22. The authors propose that this prodrug/enzyme combination could be exploited therapeutically in a manner analogous to approaches currently under investigation with the combinations of ganciclovir/herpes simplex virus thymidine kinase and 5-fluorocytosine/cytosine deaminase. van Pelt et al. demonstrated that a 55 kD human liver carboxylesterase inhibits the invasion of Plasmodium falciparum malaria sporozoites into primary human hepatocytes in culture. J Hepatol (1997) 27(4):688-698.

Carboxylesterases have also been found to be of importance in the detoxification of drugs, pesticides

and other xenobiotics. Purified human liver carboxylesterases have been shown to be involved in the metabolism of various drugs including cocaine and heroin. Prindel *et al.* describe the purification and cloning of a broad substrate specificity human liver carboxylesterase which catalyzes the hydrolysis of cocaine and heroin and which may play an important role in the degradation of these drugs in human tissues. J. Biol. Chem. (1997) 6:272(23):14769-14775. Brzenzinski *et al.* describe a spectrophotometric competitive inhibition assay used to identify drug or environmental esters that are metabolized by carboxylesterases. Drug Metab Dispos (1997) 25(9):1089-1096.

In light of the important physiological roles played by carboxylesterases, efforts are being undertaken by both industry and academia to identify new, native carboxylesterase homologs. We herein describe the identification and characterization of a novel polypeptide having homology to carboxylesterase, designated herein as PRO873.

#### 40. PRO940

CD33 is a cell-surface protein that is a member of the sialoadhesin family of proteins that are capable of mediating sialic-acid dependent binding with distinct specificities for both the type of sialic acid and its linkage to subterminal sugars. CD33 is specifically expressed in early myeloid and some monocyte cell lineages and has been shown to be strongly associated with various myeloid tumors including, for example, acute non-lymphocytic leukemia (ANLL). As such, CD33 has been suggested as a potential target for the treatment of cancers associated with high level expression of the protein. There is, therefore, significant interest in the identification of novel polypeptides having homology to CD33. In fact, one CD33 homolog (designated CD33L) has already been identified and described (see Takei *et al.*, Cytogenet. Cell Genet. 78:295-300 (1997)). We herein describe the identification of another novel polypeptide having homology to CD33, designated herein as PRO940. The novel polypeptide described herein also exhibits significant homology to the human OB binding proteins designated HSU71382\_1 and HSU71383\_1 in the Dayhoff database (version 35.45 SwissProt 35).

#### 41. PRO941

Cadherins are a large family of transmembrane proteins. Cadherins comprise a family of calcium-dependent glycoproteins that function in mediating cell-cell adhesion in virtually all solid tissues of multicellular organisms. At least cadherins 1-13 as well as types B, E, EP, M, N, P and R have been identified and characterized. Among the functions cadherins are known for, with some exceptions, are that cadherins participate in cell aggregation and are associated with cell-cell adhesion sites. Recently, it has been reported that while all cadherins share multiple repeats of a cadherin specific motif believed to correspond to folding of extracellular domains, members of the cadherin superfamily have divergent structures and, possibly, functions. In particular it has been reported that members of the cadherin superfamily are involved in signal transduction. See, Suzuki, J. Cell Biochem., 61(4):531-542 (1996). Cadherins are further described in Tanihara *et al.*, J. Cell Sci., 107(6):1697-1704 (1994), Aberle *et al.*, J. Cell Biochem., 61(4):514-523 (1996) and Tanihara *et al.*, Cell

Adhes. Commun., 2(1):15-26 (1994). We herein describe the identification and characterization of a novel polypeptide having homology to a cadherin protein, designated herein as PRO941.

42. PRO944

Clostridium perfringens enterotoxin (CPE) is considered to be the virulence factor responsible for causing the symptoms of *C. perfringens* type A food poisoning and may also be involved in other human and veterinary illnesses (McClane, *Toxicon*. 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the Clostridium perfringens enterotoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell. cDNAs encoding the CPE-R protein have been identified characterized in both human and mouse (Katahira et al., *J. Cell Biol.* 136:1239-1247 (1997) and Katahira et al., *J. Biol. Chem.* 272:26652-26658 (1997)). Since the CPE toxin has been reported to cause a variety of illnesses in mammalian hosts and those illnesses are initiated by binding of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We herein describe the identification and characterization of a novel polypeptide having homology to the CPE-R, designated herein as PRO944.

43. PRO983

Membrane-bound proteins include not only cell-surface membrane-bound proteins, but also proteins that are found on the surface of intracellular vesicles. These vesicles are involved in exocytosis, which is the fusion of secretory vesicles with the cellular plasma membrane, and have two main functions. One is the discharge of the vesicle contents into the extracellular space, and the second is the incorporation of new proteins and lipids into the plasma membrane itself. Exocytosis can be either constitutive or regulated. All eukaryotic cells exhibit constitutive exocytosis, which is marked by the immediate fusion of the secretory vesicle after formation. In contrast, regulated exocytosis results in the accumulation of the secretory vesicles that fuse with the plasma membrane upon receipt of an appropriate signal by vesicle-associated membrane proteins. Usually, this signal is an increase in the cytosolic free  $Ca^{2+}$  concentration. However, regulated exocytosis that is independent of  $Ca^{2+}$  has been reported (see, e.g. Fujita-Yoshigaki et al. *J. Biol. Chem.* (1996) 31:271(22):13130-13134). Regulated exocytosis is crucial to many specialized cells, including neurons (neurotransmitter release from synaptic vesicles), adrenal chromaffin cells (adrenaline secretion), pancreatic acinar cells (digestive enzyme secretion), pancreatic  $\beta$ -cells (insulin secretion), mast cells (histamine secretion), mammary cells (milk protein secretion), sperm (enzyme secretion), egg cells (creation of fertilization envelope) and adipocytes (insertion of glucose transporters into the plasma membrane).

Disorders involving exocytosis are known. For example, inflammatory mediator release from mast cells leads to a variety of disorders, including asthma. Similarly, Chediak-Higashi Syndrome (CHS) is a rare autosomal recessive disease in which neutrophils, monocytes and lymphocytes contain giant cytoplasmic granules. Accordingly, the proteins involved in exocytosis are of paramount interest and efforts are being undertaken by both industry and academia to identify new, vesicle-associated proteins. For example, Skehel et

al. identified a 33-kilodalton membrane protein in *Aplysia*, termed VAP-33, which is required for the exocytosis of neurotransmitter. *Science* (1995) 15:269(5230):1580-1583, and *Neuropharmacology* (1995) 34(11):1379-1385. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel vesicle-associated membrane proteins. It is an object of the invention to provide proteins having homology to the vesicle associated protein, VAP-33, designated herein as PRO983.

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#### 44. PRO1057

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized. The mammalian protease enzymes play important roles in many different biological processes including, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

In light of the important physiological roles played by protease enzymes, efforts are currently being undertaken by both industry and academia to identify new, native protease homologs. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe the identification of novel polypeptides having homology to various protease enzymes, designated herein as PRO1057 polypeptides.

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#### 45. PRO1071

Thrombospondin-1 is a trimeric high molecular weight glycoprotein that is released from platelet alpha-granules in response to thrombin stimulation and that is also a transient component of the extracellular matrix in developing and repairing tissues (Adams, *Int. J. Biochem. Cell Biol.* 29:861-865 (1997) and Qian et al., *Proc. Soc. Exp. Biol. Med.* 212:199-207 (1996)). A variety of factors regulate thrombospondin expression and the protein is degraded by both extracellular and intracellular routes. Thrombospondin-1 functions as a cell adhesion molecule and also modulates cell movement, cell proliferation, neurite outgrowth and angiogenesis. As such, there is substantial interest in identifying novel polypeptides having homology to thrombospondin. We herein describe the identification and characterization of a novel polypeptide having homology to thrombospondin, designated herein as PRO1071.

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#### 46. PRO1072

Studies have reported that the redox state of the cell is an important determinant of the fate of the cell. Furthermore, reactive oxygen species have been reported to be cytotoxic, causing inflammatory disease, including tissue necrosis, organ failure, atherosclerosis, infertility, birth defects, premature aging, mutations and malignancy. Thus, the control of oxidation and reduction is important for a number of reasons, including the

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control and prevention of strokes, heart attacks, oxidative stress, hypertension and may be associated with the development of malignancies. The levels of antioxidant enzymes, such as reductases, which catalyze the conversion of reactive oxygen species to water have been shown to be low in cancer cells. In particular, malignant prostate epithelium may have lowered expression of such antioxidant enzymes [Baker et al., *Prostate* 32(4):229-233 (1997)]. In this regard, reductases, are of interest. In addition, the transcription factors, NF-kappa B and AP-1, are known to be regulated by redox state and to affect the expression of a large variety of genes thought to be involved in the pathogenesis of AIDS, cancer, atherosclerosis and diabetic complications. Publications further describing this subject matter include Engman et al., *Anticancer Res. (Greece)*, 17:4599-4605 (1997), Kelsey, et al., *Br. J. Cancer*, 76(7):852-854 (1997); Friedrich and Weiss, *J. Theor. Biol.*, 187(4):529-40 (1997) and Pieulle, et al., *J. Bacteriol.*, 179(18):5684-92 (1997). Given the physiological importance of redox reactions *in vivo*, efforts are currently being under taken to identify new, native proteins which are involved in redox reactions. We describe herein the identification of a novel polypeptide which has sequence similarity to reductase enzymes, designated herein as PRO1072.

#### 47. PRO1075

Protein disulfide isomerase is an enzymatic protein which is involved in the promotion of correct refolding of proteins through the establishment of correct disulfide bond formation. Protein disulfide isomerase was initially identified based upon its ability to catalyze the renaturation of reduced denatured RNase (Goldberger et al., *J. Biol. Chem.* 239:1406-1410 (1964) and Epstein et al., *Cold Spring Harbor Symp. Quant. Biol.* 28:439-449 (1963)). Protein disulfide isomerase has been shown to be a resident enzyme of the endoplasmic reticulum which is retained in the endoplasmic reticulum via a -KDEL or -HDEL amino acid sequence at its C-terminus.

Given the importance of disulfide bond-forming enzymes and their potential uses in a number of different applications, for example in increasing the yield of correct refolding of recombinantly produced proteins, efforts are currently being undertaken by both industry and academia to identify new, native proteins having homology to protein disulfide isomerase. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel protein disulfide isomerase homologs. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. We herein describe a novel polypeptide having homology to protein disulfide isomerase, designated herein as PRO1075.

#### 48. PRO181

In *Drosophila*, the dorsal-ventral polarity of the egg chamber depends on the localization of the oocyte nucleus and the gurken RNA to the dorsal-anterior corner of the oocyte. Gurken protein presumably acts as a ligand for the *drosophila* EGF receptor (torpedo/DER) expressed in the somatic follicle cells surrounding the oocyte. Cornichon is a gene required in the germline for dorsal-ventral signaling (Roth et al., *Cell* 81:967-978 (1995)). Cornichon, gurken and torpedo also function in an earlier signaling event that establishes posterior

follicle cell fates and specifies the anterior-posterior polarity of the egg chamber. Mutations in any or all of these genes prevent the formation of a correctly polarized microtubule cytoskeleton required for proper localization of the anterior and posterior determinants bicoid and oskar and for the asymmetric positioning of the oocyte nucleus. Thus, it is clear that the cornichon gene product plays an important role in early development. We herein describe the identification and characterization of a novel polypeptide having homology to the cornichon protein, designated herein as PRO181.

49. **PRO195**

Efforts are currently being undertaken to identify and characterize novel transmembrane proteins. We herein describe the identification and characterization of a novel transmembrane polypeptide, designated herein as PRO195.

50. **PRO865**

Efforts are currently being undertaken to identify and characterize novel secreted proteins. We herein describe the identification and characterization of a novel secreted polypeptide, designated herein as PRO865.

51. **PRO827**

VLA-2 is a cell-surface integrin protein that has been identified and characterized in a number of mammalian organisms, including both mouse and human. VLA-2 has been shown to be a receptor on the surface of cells for echovirus-1 (EV-1) which mediates infection of VLA-2-expressing cells by EV-1 (Zhang et al., Virology 235(2):293-301 (1997) and Bergelson et al., Science 255:1718-1720 (1992)). VLA-2 has also been shown to mediate the interaction of collagen with endothelium during *in vitro* vascular tube formation (Jackson et al., Cell Biol. Int. 18(9):859-867 (1994)). Various other integrin proteins that share various degrees of amino acid sequence homology with VLA-2 have been identified and characterized in a variety of mammalian organism. These integrins have been reported to play important roles in a variety of different physiological functions. Therefore, there is significant interest in identifying novel polypeptides having homology to one or more of the integrin proteins. We herein describe the identification and characterization of a novel polypeptide having homology to VLA-2 integrin protein, designated herein as PRO827.

52. **PRO1114**

Many important cytokine proteins have been identified and characterized and shown to signal through specific cell surface receptor complexes. For example, the class II cytokine receptor family (CRF2) includes the interferon receptors, the interleukin-10 receptor and the tissue factor CRFB4 (Spencer et al., J. Exp. Med. 187:571-578 (1998) and Kotenko et al., EMBO J. 16:5894-5903 (1997)). Thus, the multitude of biological activities exhibited by the various cytokine proteins is absolutely dependent upon the presence of cytokine receptor proteins on the surface of target cells. There is, therefore, a significant interest in identifying and characterizing novel polypeptides having homology to one or more of the cytokine receptor family. We herein

describe the identification and characterization of a novel polypeptide having homology to cytokine receptor family-4 proteins, designated herein as PRO1117.

Interferons (IFNs) encompass a large family of secreted proteins occurring in vertebrates. Although they were originally named for their antiviral activity, growing evidence supports a critical role for IFNs in cell growth and differentiation (Jaramillo et al., Cancer Investigation 13(3):327-338 (1995)). IFNs belong to a class of negative growth factors having the ability to inhibit the growth of a wide variety of cells with both normal and transformed phenotypes. IFN therapy has been shown to be beneficial in the treatment of human malignancies such as Kaposi's sarcoma, chronic myelogenous leukemia, non-Hodgkin's lymphoma, and hairy cell leukemia as well as in the treatment of infectious diseases such as hepatitis B (Gamliel et al., Scanning Microscopy 2(1):485-492 (1988), Einhorn et al., Med. Oncol. & Tumor Pharmacother. 10:25-29 (1993), Ringenberg et al., Missouri Medicine 85(1):21-26 (1988), Saracco et al., Journal of Gastroenterology and Hepatology 10:668-673 (1995), Gonzalez-Mateos et al., Hepato-Gastroenterology 42:893-899 (1995) and Malaguarnera et al., Pharmacotherapy 17(5):998-1005 (1997)).

Interferons can be classified into two major groups based upon their primary sequence. Type I interferons, IFN- $\alpha$  and IFN- $\beta$ , are encoded by a superfamily of intronless genes consisting of the IFN- $\alpha$  gene family and a single IFN- $\beta$  gene that are thought to have arisen from a common ancestral gene. Type I interferons may be produced by most cell types. Type II IFN, or IFN- $\gamma$ , is restricted to lymphocytes (T cells and natural killer cells) and is stimulated by nonspecific T cell activators or specific antigens *in vivo*.

Although both type I and type II IFNs produce similar antiviral and antiproliferative effects, they act on distinct cell surface receptors, wherein the binding is generally species specific (Langer et al., Immunol. Today 9:393-400 (1988)). Both IFN- $\alpha$  and IFN- $\beta$  bind competitively to the same high affinity type I receptor, whereas IFN- $\gamma$  binds to a distinct type II receptor. The presence and number of IFN receptors on the surface of a cell does not generally reflect the sensitivity of the cell to IFN, although it is clear that the effects of the IFN protein is mediated through binding to a cell surface interferon receptor. As such, the identification and characterization of novel interferon receptor proteins is of extreme interest.

We herein describe the identification and characterization of novel interferon receptor polypeptides, designated herein as "PRO1114 interferon receptor" polypeptides. Thus, the PRO1114 polypeptides of the present invention represents a novel cell surface interferon receptor.

### 53. PRO237

Carbonic anhydrase is an enzymatic protein that which aids carbon dioxide transport and release in the mammalian blood system by catalyzing the synthesis (and the dehydration) of carbonic acid from (and to) carbon dioxide and water. Thus, the actions of carbonic anhydrase are essential for a variety of important physiological reactions in the mammal. As such, there is significant interest in the identification and characterization of novel polypeptides having homology to carbonic anhydrase. We herein describe the identification and characterization of a novel polypeptide having homology to carbonic anhydrase, designated herein as PRO237.



54. PRO541

Numerous trypsin inhibitory proteins have been identified and characterized (see, e.g., Yamakawa et al., Biochim. Biophys. Acta 1395:202-208 (1998) and Mizuki et al., Mammalian Genome 3:274-280 (1992)). Trypsin inhibitor proteins play important roles in a variety of different physiological and biological pathways and are specifically involved in such processes as the regulation of protein degradation, digestion, and the like.

- 5 Given the important roles played by such enzymatic proteins, there is significant interest in identifying and characterizing novel polypeptides having homology to known trypsin inhibitor proteins. We herein describe the identification and characterization of a novel polypeptide having homology to a trypsin inhibitor protein, designated herein as PRO541.

10 55. PRO273

Leukocytes include monocytes, macrophages, basophils, and eosinophils and play an important role in the immune response. These cells are important in the mechanisms initiated by T and/or B lymphocytes and secrete a range of cytokines which recruit and activate other inflammatory cells and contribute to tissue destruction.

- 15 Thus, investigation of the regulatory processes by which leukocytes move to their appropriate destination and interact with other cells is critical. Currently, leukocytes are thought to move from the blood to injured or inflamed tissues by rolling along the endothelial cells of the blood vessel wall. This movement is mediated by transient interactions between selectins and their ligands. Next, the leukocyte must move through the vessel wall and into the tissues. This diapedesis and extravasation step involves cell activation which  
20 promotes a more stable leukocyte-endothelial cell interaction, again mediated by integrins and their ligands.

- Chemokines are a large family of structurally related polypeptide cytokines. These molecules stimulate leukocyte movement and may explain leukocyte trafficking in different inflammatory situations. Chemokines mediate the expression of particular adhesion molecules on endothelial cells, and they produce chemoattractants which activate specific cell types. In addition, the chemokines stimulate proliferation and regulate activation of  
25 specific cell types. In both of these activities, chemokines demonstrate a high degree of target cell specificity.

- The chemokine family is divided into two subfamilies based on whether two amino terminal cysteine residues are immediately adjacent (C-C) or separated by one amino acid (C-X-C). Chemokines of the C-X-C family generally activate neutrophils and fibroblasts while the C-C chemokines act on a more diverse group of target cells including monocytes/macrophages, basophils, eosinophils and T lymphocytes. The known  
30 chemokines of both subfamilies are synthesized by many diverse cell types as reviewed in Thomson A. (1994) *The Cytokine Handbook*, 2d Ed. Academic Press, N.Y. Chemokines are also reviewed in Schall TJ (1994) *Chemotactic Cytokines: Targets for Therapeutic Development*. International Business Communications, Southborough Mass. pp 180-270; and in Paul WE (1993) *Fundamental Immunology*, 3rd Ed. Raven Press, N.Y. pp 822-826.

- 35 Known chemokines of the C-X-C subfamily include macrophage inflammatory proteins alpha and beta (MIP-1 and MIP-2), interleukin-8 (IL-8), and growth regulated protein (GRO-alpha and beta).

MIP-2 was first identified as a 6 kDa heparin binding protein secreted by the mouse macrophage cell line RAW 264.7 upon stimulation with lipopolysaccharide (LPS). MIP-2 is a member of the C-X-C (or CXC) subfamily of chemokines. Mouse MIP-2 is chemotactic for human neutrophils and induces local neutrophil infiltration when injected into the foot pads of mice. Rat MIP-2 shows 86% amino acid homology to the mouse MIP-2 and is chemotactic for rat neutrophils but does not stimulate migration of rat alveolar macrophages or human peripheral blood eosinophils or lymphocytes. In addition, the rat MIP-2 has been shown to stimulate proliferation of rat alveolar epithelial cells but not fibroblasts.

Current techniques for diagnosis of abnormalities in inflamed or diseased tissues mainly rely on observation of clinical symptoms or serological analyses of body tissues or fluids for hormones, polypeptides or various metabolites. Problems exist with these diagnostic techniques. First, patients may not manifest clinical symptoms at early stages of disease. Second, serological tests do not always differentiate between invasive diseases and genetic syndromes. Thus, the identification of expressed chemokines is important to the development of new diagnostic techniques, effective therapies, and to aid in the understanding of molecular pathogenesis.

To date, chemokines have been implicated in at least the following conditions: psoriasis, inflammatory bowel disease, renal disease, arthritis, immune-mediated alopecia, stroke, encephalitis, MS, hepatitis, and others. In addition, non-ELR-containing chemokines have been implicated in the inhibition of angiogenesis, thus indicating that these chemokines have a role in tumor vascularization and tumorigenesis.

Therefore it is the object of this invention to identify polypeptides and nucleic acids encoding the same which have sequence identity and similarity with cytokine-induced neutrophil chemoattractants, MIP-1, MIP-2, and other related proteins. The efforts of this object are provided herein.

#### 56. PROLOGUE

Beta neurexins and neuroligins are plasma membrane proteins that are displayed on the neuronal cell surface. Neuroligin 1 is enriched in synaptic plasma membranes and acts as a splice site-specific ligand for beta neurexins as described in Ichitchenko, et al., Cell, 81(3):435-443 (1995). The extracellular sequence of neuroligin 1 is composed of a catalytically inactive esterase domain homologous to acetylcholinesterase. Neuroligin 2 and 3 are similar in structure and sequence to neuroligin 1. All neuroligins contain an N-terminal hydrophobic sequence with the characteristics of a cleaved signal peptide followed by a large esterase homology domain, a highly conserved single transmembrane region, and a short cytoplasmic domain. The three neuroligins are alternatively spliced at the same position and are expressed at high levels only in the brain. Tight binding of the three neuroligins to beta neurexins is observed only for beta neurexins lacking an insert in splice site 4. Thus, neuroligins constitute a multigene family of brain-specific proteins with distinct isoforms that may have overlapping functions in mediating recognition processes between neurons, see Ichitchenko, et al., J. Biol. Chem., 271(5):2676-2682 (1996). Moreover, neurexins and neuroligins have been reported as functioning as adhesion molecules in a  $\text{Ca}^{2+}$  dependent reaction that is regulated by alternative splicing of beta neurexins, i.e., see Nguyen and Sudhof, J. Biol. Chem., 272(41):26032-26039 (1997). Given the foregoing, membrane

bound proteins are of interest. More generally, membrane-bound proteins and receptors can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound receptor proteins, particularly those having sequence identity and/or similarity with neuroligins 1, 2 and 3. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts are provided herein.

#### 57. PRO704

VIP36 is localized to the Golgi apparatus and the cell surface, and belongs to a family of legume lectin homologues in the animal secretory pathway that might be involved in the trafficking of glycoproteins, glycolipids, or both. It is further believed that VIP36 binds to sugar residues of glycosphingolipids and/or glycosylphosphatidyl-inositol anchors and might provide a link between the extracellular/luminal face of glycolipid rafts and the cytoplasmic protein segregation machinery. Further regarding VIP36, it is believed that there is a signal at its C-terminus that matches an internalization consensus sequence which confers its ability to cycle between the plasma membrane and Golgi. See, Fiedler, et al, *EMBO J.*, 13(7):1729-1740 (1994); Fiedler and Simons, *J. Cell Sci.*, 109(1):271-276 (1996); Itin, et al., *MBO J.*, 14(10):2250-2256 (1995). It is believed that VIP36 is either the same as or very closely related to the human GP36b protein. VIP36 and/or GP36b are of interest.

More generally, vesicular, cytoplasmic, extracellular and membrane-bound proteins play important roles in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information

received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment, usually at a membrane-bound receptor protein.

Secreted proteins have various industrial applications, including use as pharmaceuticals, diagnostics, biosensors and bioreactors. In fact, most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane-bound proteins, also have potential as therapeutic or diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. Membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. Transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Efforts are being undertaken by both industry and academia to identify new, native vesicular, cytoplasmic, secreted and membrane-bound receptor proteins, particularly those having sequence identity and/or similarity with VIP36. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

#### 58. PRO706

Acid phosphatase proteins are secreted proteins which dephosphorylate terminal phosphate groups under acidic pH conditions. Acid phosphatases contain a RHGXRX amino acid sequence, which is predicted to be mechanistically significant. Acid phosphatases may have important functions in the diagnosis and treatment of human diseases. For example, prostatic acid phosphatase is a secreted protein uniquely expressed in prostatic tissue and prostate cancer. The level of prostatic acid phosphatase is a potential prognostic factor for local and biochemical control in prostate cancer patients treated with radiotherapy, as described in Lankford et al., Int. J. Radiat. Oncol. Biol. Phys. 38(2): 327-333 (1997). Research suggests that a cellular immune response to prostatic acid phosphatase may mediate destructive autoimmune prostatitis, and that xenogeneic forms of prostatic acid phosphatase may prove useful for immunotherapy of prostate cancer. See Fong et al., J. Immunol. 169(7): 3113-3117 (1997). Seminal prostatic acid phosphatase levels correlate significantly with very low sperm levels (oligospermia) in individuals over 35, see Singh et al., Singapore Med. J. 37(6): 598-599 (1996). Thus,

prostatic acid phosphatase has been implicated in a variety of human diseases, and may have an important function in diagnosis and therapy of these diseases. A series of aminobenzylphosphatic acid compounds are highly potent inhibitors of prostatic acid phosphatase, as described in Beers et al., Bioorg. Med. Chem. 4(10): 1693-1701 (1996).

More generally, extracellular proteins play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins, particularly those having sequence identity with prostate acid phosphatase precursor and lysosomal acid phosphatase precursor and in some cases, those having identity with DNA found in fetal heart. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

#### 59. PRO707

Cadherins are a large family of transmembrane proteins. At least cadherins 1-13 as well as types B, E, EP, M, N, P and R have been characterized. Among the functions cadherins are known for, with some exceptions, cadherins participate in cell aggregation and are associated with cell-cell adhesion sites. Cadherins are further described in Tanihara, et al., J. Cell Sci., 107(6):1697-1704 (1994) and Tanihara, et al., Cell Adhes. Commun., 2(1):15-26 (1994). Moreover, it has been reported that some members of the cadherin superfamily are involved in general cell-cell interaction processes including transduction. See, Suzuki, J. Cell Biochem., 61(4):531-542 (1996). Therefore, novel members of the cadherin superfamily are of interest.

More generally, all novel proteins are of interest, including membrane-bound proteins. Membrane-bound proteins and receptors can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn,

received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native secreted and membrane-bound receptor proteins, particularly membrane bound proteins having identity with cadherins. The results of such efforts are provided herein.

#### 60. PRO322

Proteases are enzymatic proteins which are involved in a large number of very important biological processes in mammalian and non-mammalian organisms. Numerous different protease enzymes from a variety of different mammalian and non-mammalian organisms have been both identified and characterized, including the serine proteases which exhibit specific activity toward various serine-containing proteins. The mammalian protease enzymes play important roles in biological processes such as, for example, protein digestion, activation, inactivation, or modulation of peptide hormone activity, and alteration of the physical properties of proteins and enzymes.

Neuropsin is a novel serine protease whose mRNA is expressed in the central nervous system. Mouse neuropsin has been cloned, and studies have shown that it is involved in the hippocampal plasticity. Neuropsin has also been indicated as associated with extracellular matrix modifications and cell migrations. See, generally, Chen, et al., Neurosci., 7(2):5088-5097 (1995) and Chen, et al., J. Histochem. Cytochem., 46:313-320 (1998).

Efforts are being undertaken by both industry and academia to identify new, native membrane-bound or secreted proteins, particularly those having homology to neuropsin, serine protease, neurosin and trypsinogen. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

61. **PRO526**

Protein-protein interactions include those involved with receptor and antigen complexes and signaling mechanisms. As more is known about the structural and functional mechanisms underlying protein-protein interactions, protein-protein interactions can be more easily manipulated to regulate the particular result of the protein-protein interaction. Thus, the underlying mechanisms of protein-protein interactions are of interest to the scientific and medical community.

All proteins containing leucine-rich repeats are thought to be involved in protein-protein interactions. Leucine-rich repeats are short sequence motifs present in a number of proteins with diverse functions and cellular locations. The crystal structure of ribonuclease inhibitor protein has revealed that leucine-rich repeats correspond to beta-alpha structural units. These units are arranged so that they form a parallel beta-sheet with one surface exposed to solvent, so that the protein acquires an unusual, nonglobular shape. These two features have been indicated as responsible for the protein-binding functions of proteins containing leucine-rich repeats. See, Kobe and Deisenhofer, Trends Biochem. Sci., 19(10):415-421 (Oct. 1994).

A study has been reported on leucine-rich proteoglycans which serve as tissue organizers, orienting and ordering collagen fibrils during ontogeny and are involved in pathological processes such as wound healing, tissue repair, and tumor stroma formation. Iozzo, R. V., Crit. Rev. Biochem. Mol. Biol., 32(2):141-174 (1997). Others studies implicating leucine rich proteins in wound healing and tissue repair are De La Salle, C., et al., Vouv. Rev. Fr. Hematol. (Germany), 37(4):215-222 (1995), reporting mutations in the leucine rich motif in a complex associated with the bleeding disorder Bernard-Soulier syndrome, Chlemetson, K. J., Thromb. Haemost. (Germany), 74(1):111-116 (July 1995), reporting that platelets have leucine rich repeats and Ruoslahti, E. I., et al., WO9110727-A by La Jolla Cancer Research Foundation reporting that decorin binding to transforming growth factor $\beta$  has involvement in a treatment for cancer, wound healing and scarring. Related by function to this group of proteins is the insulin like growth factor (IGF), in that it is useful in wound-healing and associated therapies concerned with re-growth of tissue, such as connective tissue, skin and bone; in promoting body growth in humans and animals; and in stimulating other growth-related processes. The acid labile subunit (ALS) of IGF is also of interest in that it increases the half-life of IGF and is part of the IGF complex *in vivo*. ALS is further described in Leong and Baxter, Mol. Endocrinol., 6(6):870-876 (1992); Baxter, J. Biol. Chem., 264(20):11843-11848 (1989); and Khosravi, et al., J. Clin. Endocrinol. Metab., 82(12):3944-3951 (1997).

Another protein which has been reported to have leucine-rich repeats is the SLIT protein which has been reported to be useful in treating neuro-degenerative diseases such as Alzheimer's disease, nerve damage such as in Parkinson's disease, and for diagnosis of cancer, see, Artavanistsakonas, S. and Rothberg, J. M., WO9210518-A1 by Yale University. Also of interest is LIG-1, a membrane glycoprotein that is expressed specifically in glial cells in the mouse brain, and has leucine rich repeats and immunoglobulin-like domains. Suzuki, et al., J. Biol. Chem. (U.S.), 271(37):22522 (1996). Other studies reporting on the biological functions of proteins having leucine rich repeats include: Tayar, N., et al., Mol. Cell Endocrinol., (Ireland), 125(1-2):65-70 (Dec. 1996) (gonadotropin receptor involvement); Miura, Y., et al., Nippon Rinsho (Japan), 54(7):1784-1789 (July 1996) (apoptosis involvement); Harris, P. C., et al., J. Am. Soc. Nephrol., 6(4):1125-1133 (Oct. 1995)

(kidney disease involvement).

Efforts are therefore being undertaken by both industry and academia to identify new proteins having leucine rich repeats to better understand protein-protein interactions. Of particular interest are those proteins having leucine rich repeats and identity or similarity to known proteins having leucine rich repeats such as ALS. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding  
5 sequences for novel secreted and membrane-bound proteins having leucine rich repeats. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

## 62. PRO531

10 Cadherins are a large family of transmembrane proteins. Cadherins comprise a family of calcium-dependent glycoproteins that function in mediating cell-cell adhesion in virtually all solid tissues of multicellular organisms. At least cadherins 1-13 as well as types B, E, EP, M, N, P and R have been characterized. Among the functions cadherins are known for, with some exceptions, cadherins participate in cell aggregation and are associated with cell-cell adhesion sites. Recently, it has been reported that while all cadherins share multiple  
15 repeats of a cadherin specific motif believed to correspond to folding of extracellular domains, members of the cadherin superfamily have divergent structures and, possibly, functions. In particular it has been reported that members of the cadherin superfamily are involved in signal transduction. See, Suzuki, J. Cell Biochem., 61(4):531-542 (1996). Cadherins are further described in Tanihara, et al., J. Cell Sci., 107(6):1697-1704 (1994), Aberle, et al., J. Cell Biochem., 61(4):514-523 (1996) and Tanihara, et al., Cell Adhes. Commun.,  
20 2(1):15-26 (1994).

Protocadherins are members of the cadherin superfamily which are highly expressed in the brain. In some studies, protocadherins have shown cell adhesion activity. See, Sano, et al., EMBO J., 12(6):2249-2256 (1993). However, studies have also shown that some protocadherins, such as protocadherin 3 (also referred to as Pcdh3 or pc3), do not show strong calcium dependent cell aggregation activity. See, Sago, et al., Genomics,  
25 29(3):631-640 (1995) for this study and further characteristics of Pcdh3.

Therefore, novel members of the cadherin superfamily are of interest. More generally, all membrane-bound proteins and receptors are of interest. Such proteins can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation,  
30 migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor  
35 kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is



regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are therefore being undertaken by both industry and academia to identify new, native membrane bound proteins, particular those having sequence identity with protocadherins, especially 3 and 4. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. Provided herein are the results of such efforts.

### 63. PRO534

Protein disulfide isomerase is an enzymatic protein which is involved in the promotion of correct refolding of proteins through the establishment of correct disulfide bond formation. Protein disulfide isomerase was initially identified based upon its ability to catalyze the renaturation of reduced denatured RNase (Goldberger et al., *J. Biol. Chem.* 239:1406-1410 (1964) and Epstein et al., *Cold Spring Harbor Symp. Quant. Biol.* 28:439-449 (1963)). Protein disulfide isomerase has been shown to be a resident enzyme of the endoplasmic reticulum which is retained in the endoplasmic reticulum via a -KDEL or -HDEL amino acid sequence at its C-terminus. Protein disulfide isomerase and related proteins are further described in Laboissiere, et al., *J. Biol. Chem.*, 270(47):28006-28009 (1995); Jeenes, et al., *Gene*, 193(2):151-156 (1997); Koivunen, et al., *Genomics*, 42(3):397-404 (1997); and Desilva, et al., *DNA Cell Biol.*, 15(1):9-16 (1996). These studies indicate the importance of the identification of protein disulfide related proteins.

More generally, and also of interest are all novel membrane-bound proteins and receptors. Such proteins can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic

agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Given the importance of membrane bound proteins, efforts are under way to identify novel membrane bound proteins. Moreover, given the importance of disulfide bond-forming enzymes and their potential uses in a number of different applications, for example in increasing the yield of correct refolding of recombinantly produced proteins, efforts are currently being undertaken by both industry and academia to identify new, native proteins having sequence identity with protein disulfide isomerase. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel protein disulfide isomerase homologs. We herein describe a novel polypeptide having sequence identity with protein disulfide isomerase and the nucleic acids encoding the same.

#### 64. PRO697

Secreted frizzled related proteins (sFRPs) are related to the frizzled family of transmembrane receptors. The sFRPs are approximately 30 kDa in size, and each contains a putative signal sequence, a frizzled-like cysteine-rich domain, and a conserved hydrophilic carboxy-terminal domain. It has been reported that sFRPs may function to modulate Wnt signaling, or function as ligands for certain receptors. Rattner, et al., PNAS USA, 94(7):2859-2863 (1997). Therefore, sFRPs and proteins having sequence identity and/or similarity to sFRPs are of interest.

Another secreted protein of interest is any member of the family of secreted apoptosis-related proteins (SARPs). Expression of SARPs modifies the intracellular levels of beta-catenin, suggesting that SARPs interfere with the Wnt-frizzled proteins signaling pathway. Melkonyan, et al., PNAS USA, 94(25):13636-13641 (1997). Therefore, SARPs and proteins having sequence identity and/or similarity to SARPs are of interest.

In addition to sFRPs and SARPs, many extracellular proteins are of interest. Extracellular proteins play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents.

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins, particularly those having sequence identity or similarity with sFRP-2 and SARP-1. Many efforts are focused

on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

65. **PRO717**

5 Efforts are being undertaken by both industry and academia to identify new, native transmembrane receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. The results of such efforts are provided herein.

66. **PRO731**

10 Cadherins are a large family of transmembrane proteins. Cadherins comprise a family of calcium-dependent glycoproteins that function in mediating cell-cell adhesion in virtually all solid tissues of multicellular organisms. At least cadherins 1-13 as well as types B, E, EP, M, N, P and R have been characterized. Among the functions cadherins are known for, with some exceptions, cadherins participate in cell aggregation and are associated with cell-cell adhesion sites. Recently, it has been reported that while all cadherins share multiple  
15 repeats of a cadherin specific motif believed to correspond to folding of extracellular domains, members of the cadherin superfamily have divergent structures and, possibly, functions. In particular it has been reported that members of the cadherin superfamily are involved in signal transduction. See, Suzuki, J. Cell Biochem., 61(4):531-542 (1996). Cadherins are further described in Tanihara, et al., J. Cell Sci., 107(6):1697-1704 (1994), Aberle, et al., J. Cell Biochem., 61(4):514-523 (1996) and Tanihara, et al., Cell Adhes. Commun.,  
20 2(1):15-26 (1994).

Protocadherins are members of the cadherin superfamily which are highly expressed in the brain. In some studies, protocadherins have shown cell adhesion activity. See, Sano, et al., EMBO J., 12(6):2249-2256 (1993). However, studies have also shown that some protocadherins, such as protocadherin 3 (also referred to as Pcdh3 or pc3), do not show strong calcium dependent cell aggregation activity. See, Sago, et al., Genomics,  
25 29(3):631-640 (1995) for this study and further characteristics of Pcdh3.

Therefore, novel members of the cadherin superfamily are of interest. More generally, all membrane-bound proteins and receptors are of interest. Such proteins can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from  
30 other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like  
35 selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze

that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are therefore being undertaken by both industry and academia to identify new, native membrane bound proteins, particularly those having sequence identity with protocadherins, especially 4, 68, 43, 42, 3 and 5. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel membrane-bound proteins. Provided herein are the results of such efforts.

67. PRO218

Efforts are being undertaken by both industry and academia to identify new, native membrane bound proteins, particularly those having sequence identity with membrane regulator proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins.

68. PRO768

The integrins comprise a supergene family of cell-surface glycoprotein receptors that promote cellular adhesion. Each cell has numerous receptors that define its cell adhesive capabilities. Integrins are involved in a wide variety of interaction between cells and other cells or matrix components. The integrins are of particular importance in regulating movement and function of immune system cells. The platelet IIb/IIIa integrin complex is of particular importance in regulating platelet aggregation. A member of the integrin family, integrin  $\beta$ -6, is expressed on epithelial cells and modulates epithelial inflammation. Another integrin, leucocyte-associated antigen-1 (LFA-1) is important in the adhesion of lymphocytes during an immune response.

Of particular interest is H36-alpha 7, an integrin alpha chain that is developmentally regulated during myogenesis as described in Song, et al., *J. Cell Biol.*, 117(3):643-657 (1992). The expression pattern of the laminin-binding alpha 7 beta 1 integrin is developmentally regulated in skeletal, cardiac, and smooth muscle. Ziober, et al., *Mol. Biol. Cell*, 8(9):1723-1734 (1997). It has been reported that expression of the alpha 7-X1/X2 integrin is a novel mechanism that regulates receptor affinity states in a cell-specific context and may modulate integrin-dependent events during muscle development and repair. *Id.* It has further been reported that laminins promote the locomotion of skeletal myoblasts via the alpha 7 integrin receptor. In particular it was reported that alpha 7 beta 1 receptor can promote myoblast adhesion and motility on a restricted number of laminin isoforms and may be important in myogenic precursor recruitment during regeneration and differentiation. Yao, et al., *J. Cell Sci.*, 109(13):3139-3150 (1996). Spliced variants of integrin alpha 7 are also described in Leung, et al., *Biochem. Biophys. Res. Commun.*, 243(1):317-325 (1998) and Fornaro and

Languino, Matrix Biol., 16(4):185-193 (1997). Moreover, it has been reported that absence of integrin alpha 7 causes a form of muscular dystrophy. Thus integrins, particularly those related to integrin 7 and related molecules, are of interest.

In addition to the interest of integrins, more generally, all membrane-bound proteins and receptors are of interest since such proteins can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Therefore, efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. The results of such efforts, particularly those focused on identifying new polypeptides having sequence identity with integrins, are provided herein.

## 69. PRO771

Testican is a multidomain testicular proteoglycan which is expressed in numerous tissue types including, but not limited to neuromuscular tissue, the brain and reproductive tissues. Testican resembles modulators of cell social behavior such as the regulation of cell shape, adhesion, migration and proliferation. [Bonnet, F. et al., J. Biol. Chem., 271(8):4373 (1996), Perin, J.P. et al., EXS (Switzerland), 70:191 (1994), Alliel, P.M., et al., Eur. J. Biochem., 214(1):346 (1993), Charbonnier, F., et al., C. R. Seances Soc. Biol. Fil. (France), 191(1):127 (1997)]. Among other reasons, since testican has been implicated in neuronal processes and may be associated with the growth of connective tissue, testican and related molecules are of interest.

More generally, all extracellular proteins are of interest. Extracellular proteins play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted

polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

5 Secreted proteins have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted  
10 proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts, particularly those focused on identifying molecules having identity and/or similarity with testican are of interest.

70. PRO733

15 T1/ST2 is a receptor-like molecule homologous to the type I interleukin-1 receptor, believed to be involved in cell signaling. The T1/ST2 receptor and/or putative ligands are further described in Gayle, et al., J. Biol. Chem., 271(10):5784-5789 (1996), Kumar, et al., J. Biol. Chem., 270(46):27905-27913 (1995), and Mitcham, et al., J. Biol. Chem., 271(10):5777-5783 (1996). These proteins, and proteins related thereto are of interest.

20 More generally all membrane-bound proteins and receptors are of interest since they can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell  
25 receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins.  
30 Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening  
35 of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor proteins.

Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. The results of such efforts are provided herein.

71. PRO162

Pancreatitis-associated protein (PAP) is a secretory protein that is overexpressed by the pancreas during acute pancreatitis. Serum PAP concentrations have been shown to be abnormally high in patients with acute pancreatitis. Pezzilli et al., Am. J. Gastroenterol., 92(10):1887-1890 (1997).

PAP is synthesized by the pancreas due to pancreatic inflammation and has been shown to be a good serum marker for injury of the pancreas. In addition, serum PAP levels appear to strongly correlate with creatinine clearance measurements. In patients with a pancreas-kidney transplantation, PAP may prove to be a useful biological and histological marker of pancreatic graft rejection. Van der Pijl et al., Transplantation, 63(7):995-1003 (1997). Further, PAP has been shown to be useful in screening neonates for cystic fibrosis. In fact, PAP may discriminate cystic fibrosis neonates with better specificity than the current immunoreactive trypsin assay. Iovanna et al., C. R. Acad. Sci. III, 317(6):561-564.

Secreted proteins such as PAP have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents.

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7112 (1996); U.S. Patent No. 5,536,637]. The results of such efforts are presented herein.

72. PRO788

Anti-neoplastic urinary protein (ANUP) was identified as the major protein present in a fraction of human urine which exhibits antiproliferative activity against human tumor cell lines without affecting the growth of several normal diploid cell lines or tumor cells of mouse or hamster origin. Sloane et al., Biochem. J., 234(2):355-362 (1986).

ANUP is a unique cytokine that has been found in human granulocytes. The N-terminal amino acid sequence has been shown to be unique. A synthetic peptide corresponding to the first nine residues, with Cys at positions 4 and 7, was found to be an anti-tumor agent in vitro. Ridge and Sloane, Cytokine, 8(1):1-5 (1996).

Secreted proteins such as ANUP have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents.

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637].

5 73. PRO1008

Dickkopf-1 (dkk-1) is a member of a family of secreted proteins and functions in head induction. Dkk-1 is an inducer of Spemann organizer in amphibian embryos. Glinka, et al., Nature, 391(6665):357-362 (1998). Dkk-1 is a potent antagonist of Wnt signalling, suggesting that dkk genes encode a family of secreted Wnt inhibitors. Thus, dkk-1 family members and related molecules are of interest.

10 More generally, all extracellular proteins are of interest since they can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors,  
15 neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins,  
20 erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents.

~~Efforts are being undertaken by both industry and academia to identify new, native secreted proteins,~~  
particularly those related to dkk-1. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and  
25 techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts to identify molecules related to dkk-1 are provided herein.

74. PRO1012

30 Protein disulfide isomerase is an enzymatic protein which is involved in the promotion of correct refolding of proteins through the establishment of correct disulfide bond formation. Protein disulfide isomerase was initially identified based upon its ability to catalyze the renaturation of reduced denatured RNase (Goldberger et al., J. Biol. Chem. 239:1406-1410 (1964) and Epstein et al., Cold Spring Harbor Symp. Quant. Biol. 28:439-449 (1963)). Protein disulfide isomerase has been shown to be a resident enzyme of the  
35 endoplasmic reticulum which is retained in the endoplasmic reticulum via a -KDEL or -HDEL amino acid sequence at its C-terminus. Protein disulfide isomerase and related proteins are further described in Laboissiere,



et al., J. Biol. Chem., 270(47):28006-28009 (1995); Jeenes, et al., Gene, 193(2):151-156 (1997); Koivunen, et al., Genomics, 42(3):397-404 (1997); and Desilva, et al., DNA Cell Biol., 15(1):9-16 (1996). These studies indicate the importance of the identification of protein disulfide related proteins.

More generally, the identification of all extracellular and membrane-bound proteins is of interest since they play important roles in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment, usually at a membrane-bound receptor protein.

Secreted proteins have various industrial applications, including use as pharmaceuticals, diagnostics, biosensors and bioreactors. In fact, most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane-bound proteins, also have potential as therapeutic or diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. Membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. Transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Of particular interest are cellular proteins having endoplasmic reticulum (ER) retention signals. These proteins are retained in the cell and function closely with endoplasmic reticulum in protein production. Such proteins have been described previously, i.e., see Shorrosh and Dixon, Plant J., 2(1):51-58 (1992).

Efforts are being undertaken by both industry and academia to identify new, native secreted and membrane-bound receptor proteins, and in particular, cellular proteins having ER retention signals. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts, particularly the identification of novel polypeptides and nucleic acids encoding the same, which have sequence identity and similarity to protein disulfide isomerase are presented herein.

75. PRO1014

Oxygen free radicals and antioxidants appear to play an important role in the central nervous system after cerebral ischemia and reperfusion. Moreover, cardiac injury, related to ischaemia and reperfusion has been reported to be caused by the action of free radicals. Additionally, studies have reported that the redox state of the cell is a pivotal determinant of the fate of the cells. Furthermore, reactive oxygen species have been reported to be cytotoxic, causing inflammatory disease, including tissue necrosis, organ failure, atherosclerosis, infertility, birth defects, premature aging, mutations and malignancy. Thus, the control of oxidation and reduction is important for a number of reasons including for control and prevention of strokes, heart attacks, oxidative stress and hypertension. In this regard, reductases, and particularly, oxidoreductases, are of interest. Publications further describing this subject matter include Kelsey, et al., Br. J. Cancer, 76(7):852-4 (1997); Friedrich and Weiss, J. Theor. Biol., 187(4):529-40 (1997) and Pieulle, et al., J. Bacteriol., 179(18):5684-92 (1997).

In addition to reductases in particular, novel polypeptides are generally of interest. Extracellular proteins play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts, particularly those identifying polypeptides having sequence identity with reductases, and the nucleic acids encoding the same, are presented herein.

76. PRO1017

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Sulfotransferases are enzymes which transfer sulfate from a sulfate donor to acceptor substrates, particularly those containing terminal glucuronic acid. The HNK-1 carbohydrate epitope is expressed on several neural adhesion glycoproteins and a glycolipid, and is involved in cell interactions. The

glucuronyltransferase and sulfotransferase are considered to be the key enzymes in the biosynthesis of this epitope because the rest of the structure occurs often in glycoconjugates. HNK-1 sulfotransferase is further described in Bakker, H., et al., *J. Biol. Chem.*, 272(47):29942-29946 (1997).

In addition to HNK-1 sulfotransferase, and novel proteins related thereto, all novel proteins are of interest. Extracellular and membrane-bound proteins play important roles in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment, usually at a membrane-bound receptor protein.

Secreted proteins have various industrial applications, including use as pharmaceuticals, diagnostics, biosensors and bioreactors. In fact, most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane-bound proteins, also have potential as therapeutic or diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. Membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. Transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Efforts are being undertaken by both industry and academia to identify new, native secreted and membrane-bound receptor proteins, particularly those having sequence identity with HNK-1 sulfotransferase. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts are provided herein.

#### 77. PRO474

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Glucose dehydrogenase functions in the oxidation of glucose to gluconate to generate metabolically useful energy. The regulation of the PQQ-linked glucose dehydrogenase in different organisms is reviewed in Neijssel, et al., *Antonie Van Leeuwenhoek*, 56(1):51-61 (1989). Glucose dehydrogenase

functions as an auxiliary energy generating mechanism, because it is maximally synthesized under conditions of energy stress. In addition to molecules related to glucose dehydrogenase, all novel proteins are of interest. Extracellular and membrane-bound proteins play important roles in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment, usually at a membrane-bound receptor protein.

Secreted proteins have various industrial applications, including use as pharmaceuticals, diagnostics, biosensors and bioreactors. In fact, most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane-bound proteins, also have potential as therapeutic or diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. Membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. Transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Efforts are being undertaken by both industry and academia to identify novel native secreted and membrane-bound receptor proteins, and particularly cellular proteins and those related to dehydrogenase or oxidoreductase. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted and membrane-bound receptor proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., Proc. Natl. Acad. Sci., 93:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts are presented herein.

#### 78. PRO1031

It has been reported that the cytokine interleukin 17 (IL-17) stimulates epithelial, endothelial, and fibroblastic cells to secrete cytokines such as IL-6, IL-8, and granulocyte-colony-stimulating factor, as well as prostaglandin E2. Moreover, it has been shown that when cultured in the presence of IL-17, fibroblasts could sustain proliferation of CD34+ preferential maturation into neutrophils. Thus it has been suggested that IL-17 constitutes an early initiator of the T cell-dependent inflammatory reaction and/or an element of the cytokine network that bridges the immune system to hematopoiesis. See, Yao, et al., J. Immunol., 155(12):5483-5486 (1995); Fossiez, et al., J. Exp. Med., 183(6):2593-2603 (1996); Kennedy, et al., J. Interferon Cytokine Res.,

16(8):611-617 (1996). Thus, proteins related to IL-17 are of interest.

More generally, all novel proteins are of interest. Extracellular proteins play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. These secreted polypeptides or signaling molecules normally pass through the cellular secretory pathway to reach their site of action in the extracellular environment.

Secreted proteins have various industrial applications, including pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents.

Efforts are being undertaken by both industry and academia to identify new, native secreted proteins, particularly those related to IL-17. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins. Examples of screening methods and techniques are described in the literature [see, for example, Klein et al., *Proc. Natl. Acad. Sci.*, **93**:7108-7113 (1996); U.S. Patent No. 5,536,637]. The results of such efforts are presented herein.

#### 79. PRO938

Protein disulfide isomerase is an enzymatic protein which is involved in the promotion of correct refolding of proteins through the establishment of correct disulfide bond formation. Protein disulfide isomerase was initially identified based upon its ability to catalyze the renaturation of reduced denatured RNase (Goldberger et al., *J. Biol. Chem.* **239**:1406-1410 (1964) and Epstein et al., *Cold Spring Harbor Symp. Quant. Biol.* **28**:439-449 (1963)). Protein disulfide isomerase has been shown to be a resident enzyme of the endoplasmic reticulum which is retained in the endoplasmic reticulum via a -KDEL or -HDEL amino acid sequence at its C-terminus. Protein disulfide isomerase and related proteins are further described in Laboissiere, et al., *J. Biol. Chem.*, **270**(47):28006-28009 (1995); Jeenes, et al., *Gene*, **193**(2):151-156 (1997); Koivunen, et al., *Genomics*, **42**(3):397-404 (1997); Desilva, et al., *DNA Cell Biol.*, **15**(1):9-16 (1996); Freedman, et al. *Trends in Biochem. Sci.* **19**:331-336 (1994); Bulleid, N.J. *Advances in Prot. Chem.* **44**:125-50 (1993); and Noiva, R., *Prot. Exp. and Purification* **5**:1-13 (1994). These studies indicate the importance of the identification of protein disulfide related proteins.

More generally, and also of interest are all novel membrane-bound proteins and receptors. Such proteins can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides (for instance, mitogenic factors, survival factors,

cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Given the importance of membrane bound proteins, efforts are under way to identify novel membrane bound proteins. Moreover, given the importance of disulfide bond-forming enzymes and their potential uses in a number of different applications, for example in increasing the yield of correct refolding of recombinantly produced proteins, efforts are currently being undertaken by both industry and academia to identify new, native proteins having sequence identity with protein disulfide isomerase. Many of these efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel protein disulfide isomerase homologs.

We herein describe the identification and characterization of a novel polypeptide having homology to protein disulfide isomerase.

#### 80. PRO1082

The low density lipoprotein (LDL) receptor is a membrane-bound protein that plays a key role in cholesterol homeostasis, mediating cellular uptake of lipoprotein particles by high affinity binding to its ligands, apolipoprotein (apo) B-100 and apoE. The ligand-binding domain of the LDL receptor contains 7 cysteine-rich repeats of approximately 40 amino acids, wherein each repeat contains 6 cysteines, which form 3 intra-repeat disulfide bonds. These unique structural features provide the LDL receptor with its ability to specifically interact with apo B-100 and apoE, thereby allowing for transport of these lipoprotein particles across cellular membranes and metabolism of their components. Soluble fragments containing the extracellular domain of the LDL receptor have been shown to retain the ability to interact with its specific lipoprotein ligands (Simmons et al., J. Biol. Chem. 272:25531-25536 (1997)). LDL receptors are further described in Javitt, FASEB J., 9(13):1378-1381 (1995) and Herz and Willnow, Ann. NY Acad. Sci., 737:14-19 (1994). Thus, proteins having sequence identity with LDL receptors are of interest.

More generally, all membrane-bound proteins and receptors can play an important role in the formation, differentiation and maintenance of multicellular organisms. The fate of many individual cells, e.g., proliferation, migration, differentiation, or interaction with other cells, is typically governed by information received from other cells and/or the immediate environment. This information is often transmitted by secreted polypeptides

(for instance, mitogenic factors, survival factors, cytotoxic factors, differentiation factors, neuropeptides, and hormones) which are, in turn, received and interpreted by diverse cell receptors or membrane-bound proteins. Such membrane-bound proteins and cell receptors include, but are not limited to, cytokine receptors, receptor kinases, receptor phosphatases, receptors involved in cell-cell interactions, and cellular adhesion molecules like selectins and integrins. For instance, transduction of signals that regulate cell growth and differentiation is regulated in part by phosphorylation of various cellular proteins. Protein tyrosine kinases, enzymes that catalyze that process, can also act as growth factor receptors. Examples include fibroblast growth factor receptor and nerve growth factor receptor. Of particular interest are membrane bound proteins that have type II transmembrane domains.

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are thus being undertaken by both industry and academia to identify new, native proteins, particularly membrane bound proteins including type II transmembrane bound proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. The results of such efforts are provided herein.

#### 81. PRO1083

Of particular interest are membrane bound proteins that belong to the seven transmembrane (7TM) receptor superfamily. Examples of these receptors include G-protein coupled receptors such as ion receptors. Another example of a 7TM receptor superfamily member is described in Osterhoff et al., DNA Cell Biol. 16(4):379-389 (1997).

Membrane-bound proteins and receptor molecules have various industrial applications, including as pharmaceutical and diagnostic agents. Receptor immunoadhesins, for instance, can be employed as therapeutic agents to block receptor-ligand interaction. The membrane-bound proteins can also be employed for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction.

Efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. The results of such efforts are presented herein.

#### 82. PRO200

Polypeptides involved in survival, proliferation and/or differentiation of cells are of interest. Polypeptides known to be involved in the survival, proliferation and/or differentiation of cells include VEGF and members of the bone morphogenetic protein family. Therefore, novel polypeptides which are related to either VEGF or the bone morphogenetic protein are of interest.

The heparin-binding endothelial cell-growth factor, VEGF, was identified and purified from media conditioned by bovine pituitary follicular or folliculo-stellate cells over several years ago. See Ferrara *et al.*, *Biophys. Res. Comm.* 161, 851 (1989). VEGF is a naturally occurring compound that is produced in follicular or folliculo-stellate cells (FC), a morphologically well characterized population of granular cells. The FC are stellate cells that send cytoplasmic processes between secretory cells.

5 VEGF is expressed in a variety of tissues as multiple homodimeric forms (121, 165, 189 and 206 amino acids per monomer) resulting from alternative RNA splicing. VEGF<sub>121</sub> is a soluble mitogen that does not bind heparin; the longer forms of VEGF bind heparin with progressively higher affinity. The heparin-binding forms of VEGF can be cleaved in the carboxy terminus by plasmin to release (a) diffusible form(s) of VEGF. Amino acid sequencing of the carboxy terminal peptide identified after plasmin cleavage is Arg<sub>110</sub>-Ala<sub>111</sub>. Amino  
10 terminal "core" protein, VEGF (1-110) isolated as a homodimer, binds neutralizing monoclonal antibodies (4.6.1 and 2E3) and soluble forms of FMS-like tyrosine kinase (FLT-1), kinase domain region (KDR) and fetal liver kinase (FLK) receptors with similar affinity compared to the intact VEGF<sub>165</sub> homodimer.

As noted, VEGF contains two domains that are responsible respectively for binding to the KDR and FLT-1 receptors. These receptors exist only on endothelial (vascular) cells. As cells become depleted in  
15 oxygen, because of trauma and the like, VEGF production increases in such cells which then bind to the respective receptors in order to signal ultimate biological effect. The signal then increases vascular permeability and the cells divide and expand to form new vascular pathways - vasculogenesis and angiogenesis.

Thus, VEGF is useful for treating conditions in which a selected action on the vascular endothelial cells, in the absence of excessive tissue growth, is important, for example, diabetic ulcers and vascular injuries  
20 resulting from trauma such as subcutaneous wounds. Being a vascular (artery and venus) endothelial cell growth factor, VEGF restores cells that are damaged, a process referred to as vasculogenesis, and stimulates the formulation of new vessels, a process referred to as angiogenesis.

VEGF would also find use in the restoration of vasculature after a myocardial infarct, as well as other uses that can be deduced. In this regard, inhibitors of VEGF are sometimes desirable, particularly to mitigate  
25 processes such as angiogenesis and vasculogenesis in cancerous cells.

Regarding the bone morphogenetic protein family, members of this family have been reported as being involved in the differentiation of cartilage and the promotion of vascularization and osteoinduction in preformed hydroxyapatite. Zou, et al., *Genes Dev.* (U.S.), 11(17):2191 (1997); Levine, et al., *Ann. Plast. Surg.*, 39(2):158 (1997). A number of related bone morphogenetic proteins have been identified, all members of the  
30 bone morphogenetic protein (BMP) family. Bone morphogenetic native and mutant proteins, nucleic acids encoding therefor, related compounds including receptors, host cells and uses are further described in at least: U.S. Patent Nos. 5,670,338; 5,454,419; 5,661,007; 5,637,480; 5,631,142; 5,166,058; 5,620,867; 5,543,394; 4,877,864; 5,013,649; 5,106,748; and 5,399,677. Of particular interest are proteins having homology with bone morphogenetic protein 1, a procollagen C-proteinase that plays key roles in regulating matrix deposition.

35 The present invention is predicated upon research intended to identify novel polypeptides which are related to VEGF and the BMP family, and in particular, polypeptides which have a role in the survival,



proliferation and/or differentiation of cells. While the novel polypeptides are not expected to have biological activity identical to the known polypeptides to which they have homology, the known polypeptide biological activities can be used to determine the relative biological activities of the novel polypeptides. In particular, the novel polypeptides described herein can be used in assays which are intended to determine the ability of a polypeptide to induce survival, proliferation or differentiation of cells. In turn, the results of these assays can be used accordingly, for diagnostic and therapeutic purposes. The results of such research is the subject of the present invention.

### 83. PRO285 and PRO286

The cloning of the Toll gene of *Drosophila*, a maternal effect gene that plays a central role in the establishment of the embryonic dorsal-ventral pattern, has been reported by Hashimoto *et al.*, Cell **52**, 269-279 (1988). The *Drosophila* Toll gene encodes an integral membrane protein with an extracytoplasmic domain of 803 amino acids and a cytoplasmic domain of 269 amino acids. The extracytoplasmic domain has a potential membrane-spanning segment, and contains multiple copies of a leucine-rich segment, a structural motif found in many transmembrane proteins. The Toll protein controls dorsal-ventral patterning in *Drosophila* embryos and activates the transcription factor Dorsal upon binding to its ligand Spätzle. (Morisato and Anderson, Cell **76**, 677-688 (1994).) In adult *Drosophila*, the Toll/Dorsal signaling pathway participates in the anti-fungal immune response. (Lenaitre *et al.*, Cell **86**, 973-983 (1996).)

A human homologue of the *Drosophila* Toll protein has been described by Medzhitov *et al.*, Nature **388**, 394-397 (1997). This human Toll, just as *Drosophila* Toll, is a type I transmembrane protein, with an extracellular domain consisting of 21 tandemly repeated leucine-rich motifs (leucine-rich region - LRR), separated by a non-LRR region, and a cytoplasmic domain homologous to the cytoplasmic domain of the human interleukin-1 (IL-1) receptor. A constitutively active mutant of the human Toll transfected into human cell lines was shown to be able to induce the activation of NF- $\kappa$ B and the expression of NF- $\kappa$ B-controlled genes for the inflammatory cytokines IL-1, IL-6 and IL-8, as well as the expression of the costimulatory molecule B7.1, which is required for the activation of native T cells. It has been suggested that Toll functions in vertebrates as a non-clonal receptor of the immune system, which can induce signals for activating both an innate and an adaptive immune response in vertebrates. The human Toll gene reported by Medzhitov *et al.*, *supra* was most strongly expressed in spleen and peripheral blood leukocytes (PBL), and the authors suggested that its expression in other tissues may be due to the presence of macrophages and dendritic cells, in which it could act as an early-warning system for infection. The public GenBank database contains the following Toll sequences: Toll1 (DNAX# HSU88540-1, which is identical with the random sequenced full-length cDNA #HUMRSC786-1); Toll2 (DNAX# HSU88878-1); Toll3 (DNAX# HSU88879-1); and Toll4 (DNAX# HSU88880-1, which is identical with the DNA sequence reported by Medzhitov *et al.*, *supra*). A partial Toll sequence (Toll5) is available from GenBank under DNAX# HSU88881-1.

Further human homologues of the *Drosophila* Toll protein, designated as Toll-like receptors (huTLRs1-5) were recently cloned and shown to mirror the topographic structure of the *Drosophila* counterpart (Rock *et*

*al.*, Proc. Natl. Acad. Sci. USA 95: 588-593 [1998]). Overexpression of a constitutively active mutant of one human TLR (Toll-protein homologue - Medzhitov *et al.*, *supra*; TLR4 - Rock *et al.*, *supra*) leads to the activation of NF- $\kappa$ B and induction of the inflammatory cytokines and constimulatory molecules. Medzhitov *et al.*, *supra*.

5 84. PRO213-1, PRO1330 and PRO1449

Cancer is characterized by the increase in the number of abnormal, or neoplastic, cells derived from a normal tissue which proliferate to form a tumor mass, the invasion of adjacent tissues by these neoplastic tumor cells, and the generation of malignant cells which eventually spread via the blood or lymphatic system to regional lymph nodes and to distant sites (metastasis). In a cancerous state a cell proliferates under conditions in which  
10 normal cells would not grow. Cancer manifests itself in a wide variety of forms, characterized by different degrees of invasiveness and aggressiveness.

Alteration of gene expression is intimately related to the uncontrolled cell growth and de-differentiation which are a common feature of all cancers. The genomes of certain well studied tumors have been found to show decreased expression of recessive genes, usually referred to as tumor suppression genes, which would  
15 normally function to prevent malignant cell growth, and/or overexpression of certain dominant genes, such as oncogenes, that act to promote malignant growth. Each of these genetic changes appears to be responsible for importing some of the traits that, in aggregate, represent the full neoplastic phenotype (Hunter, Cell 64, 1129 [1991]; Bishop, Cell 64, 235-248 [1991]).

A well known mechanism of gene (e.g. oncogene) overexpression in cancer cells is gene amplification.  
20 This is a process where in the chromosome of the ancestral cell multiple copies of a particular gene are produced. The process involves unscheduled replication of the region of chromosome comprising the gene, followed by recombination of the replicated segments back into the chromosome (Alitalo *et al.*, *Adv. Cancer Res.* 47, 235-281 [1986]). It is believed that the overexpression of the gene parallels gene amplification, i.e. is proportionate to the number of copies made.

25 Proto-oncogenes that encode growth factors and growth factor receptors have been identified to play important roles in the pathogenesis of various human malignancies, including breast cancer. For example, it has been found that the human ErbB2 gene (erbB2, also known as her2, or c-erbB-2), which encodes a 185-kd transmembrane glycoprotein receptor (p185HER2; HER2) related to the epidermal growth factor receptor (EGFR), is overexpressed in about 25% to 30% of human breast cancer (Slamon *et al.*, *Science* 235:177-182  
30 [1987]; Slamon *et al.*, *Science* 244:707-712 [1989]).

It has been reported that gene amplification of a protooncogene is an event typically involved in the more malignant forms of cancer, and could act as a predictor of clinical outcome (Schwab *et al.*, *Genes Chromosomes Cancer* 1, 181-193 [1990]; Alitalo *et al.*, *supra*). Thus, erbB2 overexpression is commonly regarded as a predictor of a poor prognosis, especially in patients with primary disease that involves axillary  
35 lymph nodes (Slamon *et al.*, [1987] and [1989], *supra*; Ravdin and Chamness, *Gene* 159:19-27 [1995]; and Hynes and Stern, *Biochem Biophys Acta* 1198: 165-184 [1994]), and has been linked to sensitivity and/or

resistance to hormone therapy and chemotherapeutic regimens, including CMF (cyclophosphamide, methotrexate, and fluoruracil) and anthracyclines (Baselga et al., Oncology 11 (3 Suppl 1): 43-48 [1997]). However, despite the association of erbB2 overexpression with poor prognosis, the odds of HER2-positive patients responding clinically to treatment with taxanes were greater than three times those of HER2-negative patients (Ibid). A recombinant humanized anti-ErbB2 (anti-HER2) monoclonal antibody (a humanized version of the murine anti-ErbB2 antibody 4D5, referred to as rhuMAb HER2 or Herceptin 7d) has been clinically active in patients with ErbB2-overexpressing metastatic breast cancers that had received extensive prior anticancer therapy. (Baselga et al., J. Clin. Oncol. 14:737-744 [1996]).

The protein Notch and its homologues are key regulatory receptors in determining the cell fate in various development processes. The protein Notch-4, also known as int-3 oncogene, was originally identified as a frequent target in mouse mammary tumor virus (MMVS). Notch-4 is believed to be a transgene which affects the differentiation capacity of stem cells and leads to neoplastic proliferation in epithelial cells. Shirayoshi et al., Genes Cells 2(3): 213-224 (1997). During embryogenesis, the expression of Notch-4 was detected in endothelial cells of blood vessels forming tissues such as the dorsal aorta, intersegmental vessels, yolk sac vessels, cephalic vessels, heart, vessels in branchial arches, and capillary plexuses. Notch-4 expression in these tissues was also associated with flk-1, the major regulatory gene of vasculogenesis and angiogenesis. Notch-4 is also upregulated in vitro during the differentiation of endothelial stem cell. The endothelial cell specific expression pattern of Notch-4, as well as its structural similarity to Notch suggest that Notch-4 is an endothelial cell specific homologue of Notch and that it may play a role in vaculogenesis and angiogenesis.

85. PRO298

Efforts are being undertaken by both industry and academia to identify new, native receptor proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel receptor proteins. We herein describe the identification and characterization of novel transmembrane polypeptides, designated herein as PRO298 polypeptides.

86. PRO337

Neuronal development in higher vertebrates is characterized by processes that must successfully navigate distinct cellular environment en route to their synaptic targets. The result is a functionally precise formation of neural circuits. The precision is believed to result from mechanisms that regulate growth cone pathfinding and target recognition, followed by latter refinement and remodeling of such projections by events that require neuronal activity, Goodman and Shatz, Cell/Neuron [Suppl.] 72(10): 77-98 (1993). It is further evident that different neurons extend nerve fibers that are biochemically distinct and rely on specific guidance cues provided by cell-cell, cell-matrix, and chemotrophic interactions to reach their appropriate synaptic targets, Goodman et al., supra.

One particular means by which diversity of the neuronal cell surface may be generated is through differential expression of cell surface proteins referred to as cell adhesion molecules (CAMs). Neuronally

expressed CAMs have been implicated in diverse developmental processes, including migration of neurons along radial glial cells, providing permissive or repulsive substrates for neurite extension, and in promoting the selective fasciculation of axons in projectional pathways. Jessel, *Neuron* 1: 3-13 (1988); Edelman and Crossin, *Annu. Rev. Biochem.* 60: 155-190 (1991). Interactions between CAMs present on the growth cone membrane and molecules on opposing cell membranes or in the extracellular matrix are thought to provide the specific guidance cues that direct nerve fiber outgrowth along appropriate projectional pathways. Such interactions are likely to result in the activation of various second messenger systems within the growth cone that regulate neurite outgrowth. Doherty and Walsh, *Curr. Opin Neurobiol.* 2: 595-601 (1992).

In higher vertebrates, most neural CAMs have been found to be members of three major structural families of proteins: the integrins, the cadherins, and the immunoglobulin gene superfamily (IgSF). Jessel, *supra.*; Takeichi, *Annu. Rev. Biochem.* 59: 237-252 (1990); Reichardt and Tomaselli, *Annu. Rev. Neurosci.* 14: 531-570 (1991). Cell adhesion molecules of the IgSF (or Ig-CAMs), in particular, constitute a large family of proteins frequently implicated in neural cell interactions and nerve fiber outgrowth during development, Salzer and Colman, *Dev. Neurosci.* 11: 377-390 (1989); Brummendorf and Rathjen, *J. Neurochem.* 61: 1207-1219 (1993). However, the majority of mammalian Ig-CAMs appear to be too widely expressed to specify navigational pathways or synaptic targets suggesting that other CAMs, yet to be identified, have role in these more selective interactions of neurons.

Many of the known neural Ig-CAMs have been found to be attached to the plasma membrane via a glycosylphosphatidylinositol (GPI) anchor. Additionally, many studies have implicated GPI-anchored proteins in providing specific guidance cues during the outgrowth on neurons in specific pathways. In studies of the grasshopper nervous system, treatment of embryos with phosphatidylinositol-specific phospholipase C (PIPLC), which selectively removes GPI-anchored proteins from the surfaces of cells, resulted in misdirection and faulty navigation among subsets of pioneering growth cones, as well as inhibited migratory patterns of a subset of early neurons, Chang et al., *Devel.* 114: 507-519 (1992). The projection of retinal fibers to the optic tectum appears to depend, in part, on a 33 kDa GPI-anchored protein, however, the precise nature of this protein is unknown. Stahl et al., *Neuron* 5: 735-743 (1990).

The expression of various GPI-anchored proteins has been characterized amongst the different populations of primary rat neurons amongst dorsal root ganglion, sympathetic neurons of the cervical ganglion, sympathetic neurons of the superior cervical ganglion, and cerebellar granule neurons. Rosen et al., *J. Cell Biol.* 117: 617-627 (1992). In contrast to the similar pattern of total membrane protein expression by these different types of neurons, striking differences were observed in the expression of GPI-anchored proteins between these neurons. Recently, a 65 kDa protein band known as neurotrimin was discovered and found to be differentially expressed by primary neurons (Rosen et al., *supra*), and restricted to the nervous system and found to be the most abundant and earliest expressed of the GPI-anchored species in the CNS. Struyk et al., *J. Neuroscience* 15(3): 2141-2156 (1995). The discovery of neurotrimin has further lead to the identification of a family of IgSF members, each containing three Ig-like domains that share significant amino acid identity, now termed IgLON. Struyk et al., *supra*; Pimenta et al., *Gene* 170(2): 189-95 (1996).

Additional members of the IgLON subfamily include opiate binding cell adhesion molecule (OBCAM), Schofield et al., EMBO J. 8: 489-495 (1989); limbic associated membrane protein (LAMP), Pimenta et al., supra; CEPU-1; GP55, Wilson et al., J. Cell Sci. 109: 3129-3138 (1996); Eur. J. Neurosci. 9(2): 334-41 (1997); and AvGp50, Hancox et al., Brain Res. Mol. Brain Res. 44(2): 273-85 (1997).

While the expression of neurotrimin appears to be widespread, it does appear to correlated with the development of several neural circuits. For example, between E18 and P10, neurotrimin mRNA expression within the forebrain is maintained at high levels in neurons of the developing thalamus, cortical subplate, and cortex, particularly laminae V and VI (with less intense expression in II, II, and IV, and minimal expression in lamina I). Cortical subplate neurons may provide an early, temporary scaffold for the ingrowing thalamic afferents en route to their final synaptic targets in the cortex. Allendoerfer and Shatz, Annu. Rev. Neurosci. 17: 185-218 (1994). Conversely, subplate neurons have been suggested to be required for cortical neurons from layer V to select VI to grow into the thalamus, and neurons from layer V to select their targets in the colliculus, pons, and spinal cord (McConnell et al., J. Neurosci. 14: 1892-1907 (1994). The high level expression of neurotrimin in many of these projections suggests that it could be involved in their development.

In the hindbrain, high levels of neurotrimin message expression were observed within the pontine nucleus and by the internal granule cells and Purkinje cells of the cerebellum. The pontine nucleus received afferent input from a variety of sources including corticopontine fibers of layer V, and is a major source of afferent input, via mossy fibers, to the granule cells which, in turn, are a major source of afferent input via parallel fibers to Purkinje cells. [Palay and Chan-Palay, The cerebellar cortex: cytology and organization. New York: Springer (1974)]. High level expression of neurotrimin these neurons again suggests potential involvement in the establishment of these circuits.

Neurotrimin also exhibits a graded expression pattern in the early postnatal striatum. Increased neurotrimin expression is found overlying the dorsolateral striatum of the rat, while lesser hybridization intensity is seen overlying the ventromedial striatum. Struyk et al., supra. This region of higher neurotrimin hybridization intensity does not correspond to a cytoarchitecturally differentiable region, rather it corresponds to the primary area of afferent input from layer VI of the contralateral sensorimotor cortex (Gerfen, Nature 311: 461-464 (1984); Donoghue and Herkenham, Brain Res. 365: 397-403 (1986)). The ventromedial striatum, by contrast, receives the majority of its afferent input from the perirhinal and association cortex. It is noteworthy that a complementary graded pattern of LAMP expression, has been observed within the striatum, with highest expression in ventromedial regions, and lowest expression dorsolaterally. Levitt, Science 223: 299-301 (1985); Chesselet et al., Neuroscience 40: 725-733 (1991).

#### 87. PRO403

Type II transmembrane proteins, also known as single pass transmembrane proteins have an N-terminal portion lodged in the cytoplasm while the C-terminal portion is exposed to the extracellular domain.

Endothelin is a family of vasoconstrictor peptides about which much activity has been focused to better understand its basic pharmacological, biochemical and molecular biological features, including the presence and

structure of isopeptides and their genes (endothelin-1, -2 and  $\alpha_3$ ), regulation of gene expression, intracellular processing, specific endothelin converting enzymes (ECE), receptor subtypes (ET-A and ET-B), intracellular signal transduction following receptor activation, etc.

The endothelin (ET) family of peptides have potent vascular, cardiac and renal actions which may be of pathophysiological importance in many human disease states. ET-1 is expressed as an inactive 212 amino acid prepropeptide. The prepropeptide is first cleaved at Arg52-Cys53 and Arg92-Ala93 and then the carboxy terminal Lys91 and Arg92 are trimmed from the protein to generate the propeptide big ET-1.

Endothelin is generated from inactive intermediates, the big endothelins, by a unique processing event catalyzed by the zinc metalloprotease, endothelin converting enzyme (ECE). ECE was recently cloned, and its structure was shown to be a single pass transmembrane protein with a short intracellular N-terminal and a long extracellular C-terminal that contains the catalytic domain and numerous N-glycosylation sites. ECEs cleave the endothelin propeptide between Trp73 and Val74 producing the active peptide, ET, which appears to function as a local rather than a circulating hormone (Rubanyi, G.M. & Polokoff, M.A., Pharmacological Reviews 46: 325-415 (1994). Thus ECE activity is a potential site of regulation of endothelin production and a possible target for therapeutic intervention in the endothelin system. By blocking ECE activity, it is possible to stop the production of ET-1 by inhibiting the conversion of the relatively inactive precursor, big ET-1, to the physiologically active form.

Endothelins may play roles in the pathophysiology of a number of disease states including: 1) cardiovascular diseases (vasospasm, hypertension, myocardial ischemia; reperfusion injury and acute myocardial infarction, stroke (cerebral ischemia), congestive heart failure, shock, atherosclerosis, vascular thickening); 2) kidney disease (acute and chronic renal failure, glomerulonephritis, cirrhosis); 3) lung disease (bronchial asthma, pulmonary hypertension); 4) gastrointestinal disorders (gastric ulcer, inflammatory bowel diseases); 5) reproductive disorders (premature labor, dysmenorrhea, preeclampsia) and 6) carcinogenesis. Rubanyi & Polokoff, supra.

## SUMMARY OF THE INVENTION

### 1. PRO213

Applicants have identified a cDNA clone that encodes a novel polypeptide, wherein the polypeptide is designated in the present application as "PRO213".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO213 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO213 polypeptide having amino acid residues 1 to 295 of Figure 2 (SEQ ID NO:2), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another embodiment, the invention provides isolated PRO213 polypeptide. In particular, the invention provides isolated native sequence PRO213 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 295 of Figure 2 (SEQ ID NO:2).

## 2. PRO274

Applicants have identified a cDNA clone that encodes a novel polypeptide, wherein the polypeptide is designated in the present application as "PRO274".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO274 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO274 polypeptide having amino acid residues 1 to 492 of Figure 4 (SEQ ID NO:7), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the  
10 DNA39987-1184 vector deposited on April 21, 1998 as ATCC 209786 which includes the nucleotide sequence encoding PRO274.

In another embodiment, the invention provides isolated PRO274 polypeptide. In particular, the invention provides isolated native sequence PRO274 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 492 of Figure 4 (SEQ ID NO:7). An additional embodiment of the  
15 present invention is directed to an isolated extracellular domain of a PRO274 polypeptide. Optionally, the PRO274 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA39987-1184 vector deposited on April 21, 1998 as ATCC 209786.

In another embodiment, the invention provides three expressed sequence tags (EST) comprising the nucleotide sequences of SEQ ID NO:8 (herein designated as DNA17873), SEQ ID NO:9 (herein designated as  
20 DNA36157) and SEQ ID NO:10 (herein designated as DNA28929) (see Figure 5-7, respectively).

## 3. PRO300

Applicants have identified a cDNA clone that encodes a novel polypeptide, wherein the polypeptide is designated in the present application as "PRO300".

25 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO300 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO300 polypeptide having amino acid residues 1 to 457 of Figure 9 (SEQ ID NO:19), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the  
30 DNA40625-1189 vector deposited on April 21, 1998 as ATCC 209788 which includes the nucleotide sequence encoding PRO300.

In another embodiment, the invention provides isolated PRO300 polypeptide. In particular, the invention provides isolated native sequence PRO300 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 457 of Figure 9 (SEQ ID NO:19). An additional embodiment of the  
35 present invention is directed to an isolated extracellular domain of a PRO300 polypeptide. Optionally, the PRO300 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of

the DNA40625-1189 vector deposited on April 21, 1998 as ATCC 209788.

#### 4. PRO284

Applicants have identified a cDNA clone that encodes a novel transmembrane polypeptide, wherein the polypeptide is designated in the present application as "PRO284".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO284 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO284 polypeptide having amino acid residues 1 to 285 of Figure 11 (SEQ ID NO:28), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO284  
10 polypeptide having amino acid residues about 25 to 285 of Figure 11 (SEQ ID NO:28) or 1 or about 25 to X of Figure 11 (SEQ ID NO:28), where X is any amino acid from 71 to 80 of Figure 11 (SEQ ID NO:28), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA23318-1211 vector deposited on April 21, 1998 as ATCC 209787 which includes the  
15 nucleotide sequence encoding PRO284.

In another embodiment, the invention provides isolated PRO284 polypeptide. In particular, the invention provides isolated native sequence PRO284 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 285 of Figure 11 (SEQ ID NO:28). Additional embodiments of the present invention are directed to isolated PRO284 polypeptides comprising amino acids about 25 to 285 of Figure  
20 11 (SEQ ID NO:28) or 1 or about 25 to X of Figure 11 (SEQ ID NO:28), where X is any amino acid from 71 to 80 of Figure 11 (SEQ ID NO:28). Optionally, the PRO284 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA23318-1211 vector deposited on April 21, 1998 as ATCC 209787.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as  
25 DNA12982 which comprises the nucleotide sequence of SEQ ID NO:29.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA15886 which comprises the nucleotide sequence of SEQ ID NO:30.

#### 5. PRO296

30 Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to the sarcoma-amplified protein SAS, wherein the polypeptide is designated in the present application as "PRO296".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO296 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO296 polypeptide having amino acid residues 1 to 204 of Figure 15 (SEQ ID NO:36), or is complementary to such  
35 encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO296



polypeptide having amino acid residues about 35 to 204 of Figure 15 (SEQ ID NO:36) or amino acid 1 or about 35 to X of Figure 15 (SEQ ID NO:36), where X is any amino acid from 42 to 51 of Figure 15 (SEQ ID NO:36), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA39979-1213 vector deposited on April 21, 1998 as ATCC 209789 which includes

5 the nucleotide sequence encoding PRO296.

In another embodiment, the invention provides isolated PRO296 polypeptide. In particular, the invention provides isolated native sequence PRO296 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 204 of Figure 15 (SEQ ID NO:36). Additional embodiments of the present invention are directed to PRO296 polypeptides comprising amino acids about 35 to 204 of Figure 15

10 (SEQ ID NO:36) or amino acid 1 or about 35 to X of Figure 15 (SEQ ID NO:36), where X is any amino acid from 42 to 51 of Figure 15 (SEQ ID NO:36). Optionally, the PRO296 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA39979-1213 vector deposited on April 21, 1998 as ATCC 209789.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as

15 DNA23020 comprising the nucleotide sequence of SEQ ID NO:37.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA21971 comprising the nucleotide sequence of SEQ ID NO:38.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA29037 comprising the nucleotide sequence of SEQ ID NO:39.

20

#### 6. PRO329

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to a high affinity immunoglobulin F<sub>c</sub> receptor, wherein the polypeptide is designated in the present application as "PRO329".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO329 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO329 polypeptide having amino acid residues 1 to 359 of Figure 20 (SEQ ID NO:45), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the

25

30 DNA40594-1233 vector deposited on February 5, 1998 as ATCC 209617 which includes the nucleotide sequence encoding PRO329.

In another embodiment, the invention provides isolated PRO329 polypeptide. In particular, the invention provides isolated native sequence PRO329 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 359 of Figure 20 (SEQ ID NO:45). Optionally, the PRO329 polypeptide

35 is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA40594-1233 vector deposited on February 5, 1998 as ATCC 209617.

7. PRO362

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to A33 antigen and HCAR membrane-bound protein, wherein the polypeptide is designated in the present application as "PRO362".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO362 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO362 polypeptide having amino acid residues 1 to 321 of Figure 22 (SEQ ID NO:52), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO362 polypeptide having amino acid residues 1 to X of Figure 22 (SEQ ID NO:52) where X is any amino acid from amino acid 271 to 280, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA45416-1251 vector deposited on February 5, 1998 as ATCC 209620 which includes the nucleotide sequence encoding PRO362.

In another embodiment, the invention provides isolated PRO362 polypeptide. In particular, the invention provides isolated native sequence PRO362 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 321 of Figure 22 (SEQ ID NO:52). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO362 polypeptide comprising amino acids 1 to X of the amino acid sequence shown in Figure 22 (SEQ ID NO:52), wherein X is any amino acid from amino acid 271 to 280. Optionally, the PRO362 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA45416-1251 vector deposited on February 5, 1998 as ATCC 209620.

8. PRO363

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to the cell surface receptor protein HCAR, wherein the polypeptide is designated in the present application as "PRO363".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO363 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO363 polypeptide having amino acid residues 1 to 373 of Figure 24 (SEQ ID NO:59), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding a PRO363 extracellular domain polypeptide having amino acid residues 1 to X of Figure 24 (SEQ ID NO:59) where X is any amino acid from amino acid 216 to amino acid 225, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA45419-1252 vector deposited on February 5, 1998 as ATCC 209616 which includes the nucleotide sequence encoding PRO363.

In another embodiment, the invention provides isolated PRO363 polypeptide. In particular, the

invention provides isolated native sequence PRO363 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 373 of Figure 24 (SEQ ID NO:59). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO363 polypeptide, wherein that extracellular domain may comprise amino acids 1 to X of the sequence shown in Figure 24 (SEQ ID NO:59), where X is any amino acid from amino acid 216 to 225. Optionally, the PRO363 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA45419-1252 vector deposited on February 5, 1998 as ATCC 209616.

9. **PRO868**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to tumor necrosis factor receptor, wherein the polypeptide is designated in the present application as "PRO868".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO868 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO868 polypeptide having amino acid residues 1 to 655 of Figure 26 (SEQ ID NO:64), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO868 polypeptide having amino acid residues 1 to X of Figure 26 (SEQ ID NO:64), where X is any amino acid from amino acid 343 to 352 of the sequence shown in Figure 26 (SEQ ID NO:64), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In yet another aspect, the isolated nucleic acid comprises DNA encoding the PRO868 polypeptide having amino acid residues X to 655 of Figure 26 (SEQ ID NO:64), where X is any amino acid from amino acid 371 to 380 of the sequence shown in Figure 26 (SEQ ID NO:64), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA52594-1270 vector deposited on March 17, 1998 as ATCC 209679 which includes the nucleotide sequence encoding PRO868.

In another embodiment, the invention provides isolated PRO868 polypeptide. In particular, the invention provides isolated native sequence PRO868 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 655 of Figure 26 (SEQ ID NO:64). In another aspect, the isolated PRO868 polypeptide comprises amino acid residues 1 to X of Figure 26 (SEQ ID NO:64), where X is any amino acid from amino acid 343 to 352 of the sequence shown in Figure 26 (SEQ ID NO:64). In yet another aspect, the PRO868 polypeptide comprises amino acid residues X to 655 of Figure 26 (SEQ ID NO:64), where X is any amino acid from amino acid 371 to 380 of the sequence shown in Figure 26 (SEQ ID NO:64). Optionally, the PRO868 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA52594-1270 vector deposited on March 17, 1998 as ATCC 209679.

**10. PRO382**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to serine proteases, wherein the polypeptide is designated in the present application as "PRO382".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO382 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO382 polypeptide having amino acid residues 1 to 453 of Figure 28 (SEQ ID NO:69), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA45234-1277 vector deposited on March 5, 1998 as ATCC 209654 which includes the nucleotide sequence encoding PRO382.

In another embodiment, the invention provides isolated PRO382 polypeptide. In particular, the invention provides isolated native sequence PRO382 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 453 of Figure 28 (SEQ ID NO:69). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO382 polypeptide, with or without the signal peptide. Optionally, the PRO382 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA45234-1277 vector deposited on March 5, 1998 as ATCC 209654.

**11. PRO545**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to meltrin, wherein the polypeptide is designated in the present application as "PRO545".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO545 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO545 polypeptide having amino acid residues 1 to 735 of Figure 30 (SEQ ID NO:74), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 5, 1998 as ATCC 209655 which includes the nucleotide sequence encoding PRO545.

In another embodiment, the invention provides isolated PRO545 polypeptide. In particular, the invention provides isolated native sequence PRO545 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 735 of Figure 30 (SEQ ID NO:74). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO545 polypeptide. Optionally, the PRO545 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 5, 1998 as ATCC 209655.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA13217 comprising the nucleotide sequence of SEQ ID NO:75 (Figure 31).

**12. PRO617**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to CD24,

wherein the polypeptide is designated in the present application as "PRO617".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO617 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO617 polypeptide having amino acid residues 1 to 67 of Figure 33 (SEQ ID NO:85), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA48309-1280 vector deposited on March 5, 1998 as ATCC 209656 which includes the nucleotide sequence encoding PRO617.

In another embodiment, the invention provides isolated PRO617 polypeptide. In particular, the invention provides isolated native sequence PRO617 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 67 of Figure 33 (SEQ ID NO:85). Optionally, the PRO617 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA48309-1280 vector deposited on March 5, 1998 as ATCC 209656.

### 13. PRO700

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to protein disulfide isomerase, wherein the polypeptide is designated in the present application as "PRO700".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO700 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO700 polypeptide having amino acid residues 1 to 432 of Figure 35 (SEQ ID NO:90), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO700 polypeptide having amino acid residues from about 34 to 432 of Figure 35 (SEQ ID NO:90), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 31, 1998 as ATCC 209721 which includes the nucleotide sequence encoding PRO700.

In another embodiment, the invention provides isolated PRO700 polypeptide. In particular, the invention provides isolated native sequence PRO700 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 432 of Figure 35 (SEQ ID NO:90). In another embodiment, the invention provides an isolated PRO700 polypeptide absent the signal sequence, which includes an amino acid sequence comprising residues from about 34 to 432 of Figure 35 (SEQ ID NO:90). Optionally, the PRO700 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 31, 1998 as ATCC 209721.

### 14. PRO702

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to

conglutinin, wherein the polypeptide is designated in the present application as "PRO702".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO702 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO702 polypeptide having amino acid residues 1 to 277 of Figure 37 (SEQ ID NO:97), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO702 polypeptide having amino acid residues 26 to 277 of Figure 37 (SEQ ID NO:97), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA50980-1286 vector deposited on March 31, 1998 as ATCC 209717 which includes the nucleotide sequence encoding PRO702.

In another embodiment, the invention provides isolated PRO702 polypeptide. In particular, the invention provides isolated native sequence PRO702 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 277 of Figure 37 (SEQ ID NO:97). An additional embodiment of the present invention is directed to an isolated PRO702 polypeptide comprising amino acid residues 26 to 277 of Figure 37 (SEQ ID NO:97). Optionally, the PRO702 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA50980-1286 vector deposited on March 31, 1998 as ATCC 209717.

#### 15. PRO703

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to VLCAS, wherein the polypeptide is designated in the present application as "PRO703".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO703 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO703 polypeptide having amino acid residues 1 to 730 of Figure 39 (SEQ ID NO:102), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO703 polypeptide having amino acid residues from about 43 to 730 of Figure 39 (SEQ ID NO:102), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA50913-1287 vector deposited on March 31, 1998 as ATCC 209716 which includes the nucleotide sequence encoding PRO703.

In another embodiment, the invention provides isolated PRO703 polypeptide. In particular, the invention provides isolated native sequence PRO703 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 730 of Figure 39 (SEQ ID NO:102). In another embodiment, the invention provides an isolated PRO703 polypeptide absent the signal sequence, which includes an amino acid sequence comprising residues from about 43 to 730 of Figure 30 (SEQ ID NO:102). Optionally, the PRO730

polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA50913-1287 vector deposited on March 31, 1998 as ATCC 209716.

16. **PRO705**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to K-glypican, wherein the polypeptide is designated in the present application as "PRO705".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO705 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO705 polypeptide having amino acid residues 1 to 555 of Figure 41 (SEQ ID NO:109), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO705 polypeptide having amino acid residues about 24 to 555 of Figure 41 (SEQ ID NO:109), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA50914-1289 vector deposited on March 31, 1998 as ATCC 209722 which includes the nucleotide sequence encoding PRO705.

In another embodiment, the invention provides isolated PRO705 polypeptide. In particular, the invention provides isolated native sequence PRO705 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 555 of Figure 41 (SEQ ID NO:109). An additional embodiment of the present invention is directed to an isolated PRO705 polypeptide comprising amino acid residues about 24 to 555 of Figure 41 (SEQ ID NO:109). Optionally, the PRO705 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA50914-1289 vector deposited on March 31, 1998 as ATCC 209722.

17. **PRO708**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to the aryl sulfatases, wherein the polypeptide is designated in the present application as "PRO708".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO708 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO708 polypeptide having amino acid residues 1 to 515 of Figure 43 (SEQ ID NO:114), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA48296-1292 vector deposited on March 11, 1998 as ATCC 209668 which includes the nucleotide sequence encoding PRO708.

In another embodiment, the invention provides isolated PRO708 polypeptide. In particular, the invention provides isolated native sequence PRO708 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 515 of Figure 43 (SEQ ID NO:114). Another embodiment is directed

to a PRO708 polypeptide comprising residues 38-515 of the amino acid sequence shown in Figure 43 (SEQ ID NO:114). Optionally, the PRO708 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA48296-1292 vector deposited on March 11, 1998 as ATCC 209668.

18. PRO320

5 Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to fibulin, wherein the polypeptide is designated in the present application as "PRO320".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO320 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO320 polypeptide having amino acid residues 1 to 338 of Figure 45 (SEQ ID NO:119), or is complementary to such  
10 encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 11, 1998 as ATCC 209670 which includes the nucleotide sequence encoding PRO320.

In another embodiment, the invention provides isolated PRO320 polypeptide. In particular, the invention provides isolated native sequence PRO320 polypeptide, which in one embodiment, includes an amino  
15 acid sequence comprising residues 1 to 338 of Figure 45 (SEQ ID NO:119). Optionally, the PRO320 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 11, 1998 as ATCC 209670.

19. PRO324

20 Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to oxidoreductases, wherein the polypeptide is designated in the present application as "PRO324".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO324 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO324 polypeptide having amino acid residues 1 to 289 of Figure 47 (SEQ ID NO:124), or is complementary to such  
25 encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO324 polypeptide having amino acid residues 1 or about 32 to X of Figure 47 (SEQ ID NO:124), where X is any amino acid from 131 to 140, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid  
30 sequence may comprise the cDNA insert of the DNA36343-1310 vector deposited on March 30, 1998 as ATCC 209718 which includes the nucleotide sequence encoding PRO324.

In another embodiment, the invention provides isolated PRO324 polypeptide. In particular, the invention provides isolated native sequence PRO324 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 289 of Figure 47 (SEQ ID NO:124). The invention also provides isolated  
35 PRO324 polypeptide comprising residues 1 or about 32 to X of Figure 47 (SEQ ID NO:124), wherein X is any amino acid from about 131-140. Optionally, the PRO324 polypeptide is obtained or is obtainable by expressing



the polypeptide encoded by the cDNA insert of the DNA36343-1310 vector deposited on March 30, 1998 as ATCC 209718.

20. **PRO351**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to prostaticin, wherein the polypeptide is designated in the present application as "PRO351".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO351 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO351 polypeptide having amino acid residues 1 to 571 of Figure 49 (SEQ ID NO:132), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO351 polypeptide having amino acid residues about 16 to 571 of Figure 49 (SEQ ID NO:132), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA40571-1315 vector deposited on April 21, 1998 as ATCC 209784 which includes the nucleotide sequence encoding PRO351.

In another embodiment, the invention provides isolated PRO351 polypeptide. In particular, the invention provides isolated native sequence PRO351 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 571 of Figure 49 (SEQ ID NO:132). In another embodiment, the invention provides an isolated PRO351 polypeptide absent the signal sequence, which includes an amino acid sequence comprising residues from about 16 to 571 of Figure 49 (SEQ ID NO:132). Optionally, the PRO351 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA40571-1315 vector deposited on April 21, 1998 as ATCC 209784.

21. **PRO352**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to butyrophilin, wherein the polypeptide is designated in the present application as "PRO352".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO352 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO352 polypeptide having amino acid residues 1 to 316 of Figure 51 (SEQ ID NO:137), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO352 polypeptide having amino acid residues of about 29 to 316 of Figure 51 (SEQ ID NO:137), or 1 or about 29 to X of Figure 51, where X is any amino acid from 246 to 255, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA41386-1316 vector deposited on March 26, 1998 as ATCC 209703 which includes the nucleotide sequence encoding PRO352.

In another embodiment, the invention provides isolated PRO352 polypeptide. In particular, the invention provides isolated native sequence PRO352 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 316 of Figure 51 (SEQ ID NO:137). In other embodiments, the invention provides isolated PRO352 polypeptide comprising residues about 29 to 316 of Figure 51 (SEQ ID NO:137) and 1 or about 29 to X of Figure 51 (SEQ ID NO:137), wherein X is any amino acid from 246 to 255.

5 Optionally, the PRO352 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA41386-1316 vector deposited on March 26, 1998 as ATCC 209703.

## 22. PRO381

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to immunophilin proteins, wherein the polypeptide is designated in the present application as "PRO381".

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In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO381 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO381 polypeptide having amino acid residues 1 to 211 of Figure 53 (SEQ ID NO:145), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO381 polypeptide having amino acid residues about 21 to 211 of Figure 53 (SEQ ID NO:145), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA44194-1317 vector deposited on April 28, 1998 as ATCC 209808 which includes the nucleotide sequence encoding PRO381.

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In another embodiment, the invention provides isolated PRO381 polypeptide. In particular, the invention provides isolated native sequence PRO381 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 211 of Figure 53 (SEQ ID NO:145). Another embodiment is directed to a PRO381 polypeptide comprising amino acids about 21 to 211 of Figure 53 (SEQ ID NO:145). Optionally, the PRO381 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA44194-1317 vector deposited on April 28, 1998 as ATCC 209808.

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## 23. PRO386

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to the beta-2 subunit of a sodium channel, wherein the polypeptide is designated in the present application as "PRO386".

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In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO386 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO386 polypeptide having amino acid residues 1 to 215 of Figure 55 (SEQ ID NO:150), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO386 polypeptide having amino acid residues about 21 to 215 of Figure 55 (SEQ ID NO:150) or 1 or about 21 to X,

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where X is any amino acid from 156 to 165 of Figure 55 (SEQ ID NO:150), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA45415-1318 vector deposited on April 28, 1998 as ATCC 209810 which includes the nucleotide sequence encoding PRO386.

5 In another embodiment, the invention provides isolated PRO386 polypeptide. In particular, the invention provides isolated native sequence PRO386 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 215 of Figure 55 (SEQ ID NO:150). Other embodiments of the present invention are directed to PRO386 polypeptides comprising amino acids about 21 to 215 of Figure 55 (SEQ ID NO:150) and 1 or about 21 to X of Figure 55 (SEQ ID NO:150), wherein X is any amino acid from 156 to 165  
10 of Figure 55 (SEQ ID NO:150). Optionally, the PRO386 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA45415-1318 vector deposited on April 28, 1998 as ATCC 209810.

In another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequence of SEQ ID NO:151 which corresponds to an EST designated herein as DNA23350.

15 In another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequence of SEQ ID NO:152 which corresponds to an EST designated herein as DNA23536.

#### 24. PRO540

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity  
20 to LCAT, wherein the polypeptide is designated in the present application as "PRO540".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding  
a PRO540 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO540  
polypeptide having amino acid residues 1 to 412 of Figure 59 (SEQ ID NO:157), or is complementary to such  
encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under  
25 high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO540  
polypeptide having amino acid residues about 29 to 412 of Figure 59 (SEQ ID NO:157), or is complementary  
to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally,  
under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the  
DNA44189-1322 vector deposited on March 26, 1998 as ATCC 209699 which includes the nucleotide sequence  
30 encoding PRO540.

In another embodiment, the invention provides isolated PRO540 polypeptide. In particular, the  
invention provides isolated native sequence PRO540 polypeptide, which in one embodiment, includes an amino  
acid sequence comprising residues 1 to 412 of Figure 59 (SEQ ID NO:157). The invention also provides  
isolated PRO540 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues  
35 about 29 to 412 of Figure 59 (SEQ ID NO:157). Optionally, the PRO540 polypeptide is obtained or is  
obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA44189-1322 vector deposited

on March 26, 1998 as ATCC 209699.

25. **PRO615**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to synaptogyrin, wherein the polypeptide is designated in the present application as "PRO615".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO615 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO615 polypeptide having amino acid residues 1 to 224 of Figure 61 (SEQ ID NO:162), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO615  
10 polypeptide having amino acid residues X to 224 of Figure 61 (SEQ ID NO:162), where X is any amino acid from 157 to 166, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA48304-1323 vector deposited on April 28, 1998 as ATCC 209811 which includes the nucleotide sequence encoding PRO615.

15 In another embodiment, the invention provides isolated PRO615 polypeptide. In particular, the invention provides isolated native sequence PRO615 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 224 of Figure 61 (SEQ ID NO:162). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO615 polypeptide which comprises amino acid residues X to 224 of Figure 61 (SEQ ID NO:162), where X is any amino acid from 157 to 166 of Figure  
20 61 (SEQ ID NO:162). Optionally, the PRO615 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA48304-1323 vector deposited on April 28, 1998 as ATCC 209811.

26. **PRO618**

25 Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to enteropeptidase, wherein the polypeptide is designated in the present application as "PRO618".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO618 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO618 polypeptide having amino acid residues 1 to 802 of Figure 63 (SEQ ID NO:169), or is complementary to such  
30 encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding an isolated extracellular domain of a PRO618 polypeptide having amino acid residues X to 802 of Figure 63 (SEQ ID NO:169), where X is any amino acid from 63 to 72 of Figure 63 (SEQ ID NO:169), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under  
35 high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA49152-1324 vector deposited on April 28, 1998 as ATCC 209813 which includes the nucleotide sequence

encoding PRO618.

In another embodiment, the invention provides isolated PRO618 polypeptide. In particular, the invention provides isolated native sequence PRO618 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 802 of Figure 63 (SEQ ID NO:169). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO618 polypeptide comprising amino acid  
5 X to 802 where X is any amino acid from 63 to 72 of Figure 63 (SEQ ID NO:169). Optionally, the PRO618 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA49152-1324 vector deposited on April 28, 1998 as ATCC 209813.

In another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequence of SEQ ID NO:170, designated herein as DNA35597 (see Figure 64).

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27. **PRO719**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to lipoprotein lipase H, wherein the polypeptide is designated in the present application as "PRO719".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding  
15 a PRO719 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO719 polypeptide having amino acid residues 1 to 354 of Figure 66 (SEQ ID NO:178), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO719 polypeptide having amino acid residues about 17 to 354 of Figure 66 (SEQ ID NO:178), or is complementary  
20 to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA49646-1327 vector deposited on March 26, 1998 as ATCC 209705 which includes the nucleotide sequence encoding PRO719.

In another embodiment, the invention provides isolated PRO719 polypeptide. In particular, the  
25 invention provides isolated native sequence PRO719 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 354 of Figure 66 (SEQ ID NO:178). In another embodiment, the invention provides isolated PRO719 polypeptide which comprises residues about 17 to 354 of Figure 66 (SEQ ID NO:178). Optionally, the PRO719 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA49646-1327 vector deposited on March 26, 1998 as ATCC 209705.

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28. **PRO724**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to the LDL receptor, wherein the polypeptide is designated in the present application as "PRO724".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding  
35 a PRO724 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO724 polypeptide having amino acid residues 1 to 713 of Figure 68 (SEQ ID NO:183), or is complementary to such

encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding a soluble PRO724 polypeptide having amino acid residues 1 to X of Figure 68 (SEQ ID NO:183) where X is any amino acid from amino acid 437 to 446, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The above two

5 polypeptides may either possess or not possess the signal peptide. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA49631-1328 vector deposited on April 28, 1998 as ATCC 209806 which includes the nucleotide sequence encoding PRO724.

In another embodiment, the invention provides isolated PRO724 polypeptide. In particular, the invention provides isolated native sequence PRO724 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 713 of Figure 68 (SEQ ID NO:183). In another embodiment, the invention provides isolated soluble PRO724 polypeptide. In particular, the invention provides isolated soluble PRO724 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to X of Figure 68 (SEQ ID NO:183), where X is any amino acid from 437 to 446 of the sequence shown in Figure 68 (SEQ ID NO:183). Optionally, the PRO724 polypeptide is obtained or is obtainable by expressing the

10 polypeptide encoded by the cDNA insert of the DNA49631-1328 vector deposited on April 28, 1998 as ATCC 209806.

#### 29. PRO772

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to A4 protein, wherein the polypeptide is designated in the present application as "PRO772".

20

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO772 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO772 polypeptide having amino acid residues 1 to 152 of Figure 70 (SEQ ID NO:190), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under

25 high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO772 polypeptide having amino acid residues 1 to X of Figure 70 (SEQ ID NO:190), where X is any amino acid from 21 to 30 of Figure 70 (SEQ ID NO:190), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA49645-1347 vector deposited on April

30 28, 1998 as ATCC 209809 which includes the nucleotide sequence encoding PRO772.

In another embodiment, the invention provides isolated PRO772 polypeptide. In particular, the invention provides isolated native sequence PRO772 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 152 of Figure 70 (SEQ ID NO:190). Additional embodiments of the present invention are directed to PRO772 polypeptides comprising amino acids 1 to X of Figure 70 (SEQ ID

35 NO:190), where X is any amino acid from 21 to 30 of Figure 70 (SEQ ID NO:190). Optionally, the PRO772 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the

DNA49645-1347 vector deposited on April 28, 1998 as ATCC 209809.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA43509 comprising the nucleotide sequence of SEQ ID NO:191 (Figure 71).

30. **PRO852**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to various protease enzymes, wherein the polypeptide is designated in the present application as "PRO852".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO852 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO852 polypeptide having amino acid residues 1 to 518 of Figure 73 (SEQ ID NO:196), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO852 polypeptide having amino acid residues about 21 to 518 of Figure 73 (SEQ ID NO:196) or 1 or about 21 to X of Figure 73 (SEQ ID NO:196) where X is any amino acid from amino acid 461 to amino acid 470 of Figure 73 (SEQ ID NO:196), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA45493-1349 vector deposited on April 28, 1998 as ATCC 209805 which includes the nucleotide sequence encoding PRO852.

In another embodiment, the invention provides isolated PRO852 polypeptide. In particular, the invention provides isolated native sequence PRO852 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 518 of Figure 73 (SEQ ID NO:196). In other embodiments, the PRO852 comprises amino acids about 21 to amino acid 518 of Figure 73 (SEQ ID NO:196) or amino acids 1 or about 21 to X of Figure 73 (SEQ ID NO:196), where X is any amino acid from amino acid 461 to amino acid 470 of Figure 73 (SEQ ID NO:196). Optionally, the PRO852 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA45493-1349 vector deposited on April 28, 1998 as ATCC 209805.

31. **PRO853**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to reductase, wherein the polypeptide is designated in the present application as "PRO853".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO853 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO853 polypeptide having amino acid residues 1 to 377 of Figure 75 (SEQ ID NO:206), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO853 polypeptide having amino acid residues about 17 to 377 of Figure 75 (SEQ ID NO:206), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally,

under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA48227-1350 vector deposited on April 28, 1998 as ATCC 209812 which includes the nucleotide sequence encoding PRO853.

In another embodiment, the invention provides isolated PRO853 polypeptide. In particular, the invention provides isolated native sequence PRO853 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 377 of Figure 75 (SEQ ID NO:206). In another embodiment, the invention provides an isolated PRO853 polypeptide absent the signal sequence, which includes an amino acid sequence comprising residues from about 17 to 377 of Figure 75 (SEQ ID NO:206). Optionally, the PRO853 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA48227-1350 vector deposited on April 28, 1998 as ATCC 209812.

### 32. PRO860

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to neurofascin, wherein the polypeptide is designated in the present application as "PRO860".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO860 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO860 polypeptide having amino acid residues 1 to 985 of Figure 77 (SEQ ID NO:211), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO860 polypeptide having amino acid residues 1 to X of Figure 77 (SEQ ID NO:211), where X is any amino acid from 443-452 of Figure 77 (SEQ ID NO:211), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA41404-1352 vector deposited on May 6, 1998 as ATCC 209844 which includes the nucleotide sequence encoding PRO860.

In another embodiment, the invention provides isolated PRO860 polypeptide. In particular, the invention provides isolated native sequence PRO860 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 985 of Figure 77 (SEQ ID NO:211). In another embodiment, the invention provides an isolated PRO860 polypeptide which includes an amino acid sequence comprising residues 1 to X of Figure 77 (SEQ ID NO:211), where X is any amino acid residue from 443 to 452 of Figure 77 (SEQ ID NO:211). Optionally, the PRO860 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA41404-1352 vector deposited on May 6, 1998 as ATCC 209844.

### 33. PRO846

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to CMRF35, wherein the polypeptide is designated in the present application as "PRO846".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO846 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO846



polypeptide having amino acid residues 1 to 332 of Figure 79 (SEQ ID NO:216), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO846 polypeptide having amino acid residues about 18 to 332 of Figure 79 (SEQ ID NO:216) or 1 or about 18 to X of SEQ ID NO:216, where X is any amino acid from 243 to 252 of Figure 79 (SEQ ID NO:216), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA44196-1353 vector deposited on May 6, 1998 as ATCC 209847 which includes the nucleotide sequence encoding PRO846.

In another embodiment, the invention provides isolated PRO846 polypeptide. In particular, the invention provides isolated native sequence PRO846 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 332 of Figure 79 (SEQ ID NO:216). In other embodiments, the invention provides an isolated PRO846 polypeptide absent the signal sequence, which includes an amino acid sequence comprising residues from about 18 to 332 of Figure 79 (SEQ ID NO:216). Additional embodiments of the present invention are directed to an isolated PRO846 polypeptide comprising amino acid 1 or about 18 to X of Figure 79 (SEQ ID NO:216), where X is any amino acid from 243 to 252 of Figure 79 (SEQ ID NO:216). Optionally, the PRO846 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA44196-1353 vector deposited on May 6, 1998 as ATCC 209847.

#### 34. PRO862

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to lysozyme, wherein the polypeptide is designated in the present application as "PRO862".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO862 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO862 polypeptide having amino acid residues 1 to 146 of Figure 81 (SEQ ID NO:221), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO862 polypeptide having amino acid residues about 19 to 146 of Figure 81 (SEQ ID NO:221), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA52187-1354 vector deposited on May 6, 1998 as ATCC 209845 which includes the nucleotide sequence encoding PRO862.

In another embodiment, the invention provides isolated PRO862 polypeptide. In particular, the invention provides isolated native sequence PRO862 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 146 of Figure 81 (SEQ ID NO:221). In another embodiment, the invention provides an isolated PRO862 polypeptide absent the signal sequence, which includes an amino acid sequence comprising residues from about 19 to 146 of Figure 81 (SEQ ID NO:221). Optionally, the PRO862

polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA52187-1354 vector deposited on May 6, 1998 as ATCC 209845.

35. **PRO864**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence similarity to Wnt-4, wherein the polypeptide is designated in the present application as "PRO864".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO864 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO864 polypeptide having amino acid residues 1 to 351 of Figure 83 (SEQ ID NO:226), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO864 polypeptide having amino acid residues about 23 to 351 of Figure 83 (SEQ ID NO:226), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA48328-1355 vector deposited on May 6, 1998 as ATCC 209843 which includes the nucleotide sequence encoding PRO864.

In another embodiment, the invention provides isolated PRO864 polypeptide. In particular, the invention provides isolated native sequence PRO864 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 351 of Figure 83 (SEQ ID NO:226). In another embodiment, the invention provides an isolated PRO864 polypeptide absent the signal sequence, which includes an amino acid sequence comprising residues from about 23 to 351 of Figure 83 (SEQ ID NO:226). Optionally, the PRO864 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA48328-1355 vector deposited on May 6, 1998 as ATCC 209843.

36. **PRO792**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to CD23, wherein the polypeptide is designated in the present application as "PRO792".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO792 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO792 polypeptide having amino acid residues 1 to 293 of Figure 85 (SEQ ID NO:231), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO792 polypeptide having amino acid residues X to 293 of Figure 85 (SEQ ID NO:231) where X is any amino acid from 50 to 59 of Figure 85 (SEQ ID NO:231), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA56352-1358 vector deposited on May 6, 1998 as ATCC 209846 which includes the nucleotide sequence encoding PRO792.

In another embodiment, the invention provides isolated PRO792 polypeptide. In particular, the invention provides isolated native sequence PRO792 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 293 of Figure 85 (SEQ ID NO:231). An additional embodiment of the present invention is directed to PRO792 polypeptide comprising amino acids X to 293 of Figure 85 (SEQ ID NO:231), where X is any amino acid from 50 to 59 of Figure 85 (SEQ ID NO:231). Optionally, the PRO792 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA56352-1358 vector deposited on May 6, 1998 as ATCC 209846.

### 37. PRO866

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to mindin and spondin proteins, wherein the polypeptide is designated in the present application as "PRO866".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO866 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO866 polypeptide having amino acid residues 1 to 331 of Figure 87 (SEQ ID NO:236), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the isolated nucleic acid comprises DNA encoding the PRO866 polypeptide having amino acid residues about 27 to 229 of Figure 87 (SEQ ID NO:236), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA53971-1359 vector deposited on April 7, 1998 as ATCC 209750 which includes the nucleotide sequence encoding PRO866.

In another embodiment, the invention provides isolated PRO866 polypeptide. In particular, the invention provides isolated native sequence PRO866 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 331 of Figure 87 (SEQ ID NO:236). Another embodiment of the present invention is directed to PRO866 polypeptides comprising amino acids about 27 to 331 of Figure 87 (SEQ ID NO:236). Optionally, the PRO866 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA53971-1359 vector deposited on April 7, 1998 as ATCC 209750.

### 38. PRO871

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to CyP-60, wherein the polypeptide is designated in the present application as "PRO871".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO871 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO871 polypeptide having amino acid residues 1 to 472 of Figure 89 (SEQ ID NO:245), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO871 polypeptide having amino acid residues about 22 to 472 of Figure 89 (SEQ ID NO:245), or is complementary

to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA50919-1361 vector deposited on May 6, 1998 as ATCC 209848 which includes the nucleotide sequence encoding PRO871.

In another embodiment, the invention provides isolated PRO871 polypeptide. In particular, the invention provides isolated native sequence PRO871 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 472 of Figure 89 (SEQ ID NO:245). An additional embodiment of the present invention is directed to PRO871 polypeptides comprising amino acids about 22 to 472 of Figure 89 (SEQ ID NO:245). Optionally, the PRO871 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA50919-1361 vector deposited on May 6, 1998 as ATCC 209848.

#### 39. PRO873

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to carboxylesterase, wherein the polypeptide is designated in the present application as "PRO873".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO873 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO873 polypeptide having amino acid residues 1 to 545 of Figure 91 (SEQ ID NO:254), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO873 polypeptide having amino acid residues about 30 to about 545 of Figure 91 (SEQ ID NO:254), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA44179-1362 vector deposited on May 6, 1998 as ATCC 209851 which includes the nucleotide sequence encoding PRO873.

In another embodiment, the invention provides isolated PRO873 polypeptide. In particular, the invention provides isolated native sequence PRO873 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 545 of Figure 91 (SEQ ID NO:254). Additional embodiments of the present invention are directed to PRO873 polypeptides comprising amino acids about 30 to about 545 of Figure 91 (SEQ ID NO:254). Optionally, the PRO873 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA44179-1362 vector deposited on May 6, 1998 as ATCC 209851.

#### 40. PRO940

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to CD33 and OB binding protein-2, wherein the polypeptide is designated in the present application as "PRO940".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO940 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO940

polypeptide having amino acid residues 1 to 544 of Figure 93 (SEQ ID NO:259), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO940 polypeptide having amino acid residues about 16 to 544 of Figure 93 (SEQ ID NO:259) or 1 or about 16 to X of Figure 93 (SEQ ID NO:259), where X is any amino acid from 394 to 403 of Figure 93 (SEQ ID NO:259), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA54002-1367 vector deposited on April 7, 1998 as ATCC 209754 which includes the nucleotide sequence encoding PRO940.

In another embodiment, the invention provides isolated PRO940 polypeptide. In particular, the invention provides isolated native sequence PRO940 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 544 of Figure 93 (SEQ ID NO:259). Other embodiments of the present invention are directed to PRO940 polypeptides comprising amino acids about 16 to 544 of Figure 93 (SEQ ID NO:259) or 1 or about 16 to X of Figure 93 (SEQ ID NO:259), where X is any amino acid from 394 to 403 of Figure 93 (SEQ ID NO:259). Optionally, the PRO940 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA54002-1367 vector deposited on April 7, 1998 as ATCC 209754.

#### 41. PRO941

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to a cadherin protein, wherein the polypeptide is designated in the present application as "PRO941".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO941 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO941 polypeptide having amino acid residues 1 to 772 of Figure 95 (SEQ ID NO:264), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO941 polypeptide having amino acid residues about 22 to 772 of Figure 95 (SEQ ID NO:264) or 1 or about 22 to X of Figure 95 (SEQ ID NO:264), where X is any amino acid from 592 to 601 of Figure 95 (SEQ ID NO:264), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA53906-1368 vector deposited on April 7, 1998 as ATCC 209747 which includes the nucleotide sequence encoding PRO941.

In another embodiment, the invention provides isolated PRO941 polypeptide. In particular, the invention provides isolated native sequence PRO941 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 772 of Figure 95 (SEQ ID NO:264). Additional embodiments of the present invention are directed to PRO941 polypeptides which comprise amino acid about 21 to 772 of Figure 95 (SEQ ID NO:264) or 1 or about 22 to X of Figure 95 (SEQ ID NO:264), where X is any amino acid from

592 to 601 of Figure 95 (SEQ ID NO:264). Optionally, the PRO941 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA53906-1368 vector deposited on April 7, 1998 as ATCC 209747.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA6415 comprising the nucleotide sequence of Figure 96 (SEQ ID NO:265).

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#### 42. PRO944

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to Clostridium perfringens enterotoxin receptor (CPE-R), wherein the polypeptide is designated in the present application as "PRO944".

10 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO944 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO944 polypeptide having amino acid residues 1 to 211 of Figure 98 (SEQ ID NO:270), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO944  
15 polypeptide having amino acid residues about 22 to 229 of Figure 98 (SEQ ID NO:270) or amino acid 1 or about 22 to X of Figure 98 (SEQ ID NO:270) where X is any amino acid from 77 to 80 of Figure 98 (SEQ ID NO:270), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA52185-1370 vector deposited on May 14, 1998 as ATCC 209861 which  
20 includes the nucleotide sequence encoding PRO944.

In another embodiment, the invention provides isolated PRO944 polypeptide. In particular, the invention provides isolated native sequence PRO944 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 211 of Figure 98 (SEQ ID NO:270). Additional embodiments of the present invention are directed to PRO944 polypeptides comprising amino acids about 22 to 211 of Figure 98  
25 (SEQ ID NO:270) or amino acid 1 or about 22 to X of Figure 98 (SEQ ID NO:270), where X is any amino acid from 77 to 86 of Figure 98 (SEQ ID NO:270). Optionally, the PRO944 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA52185-1370 vector deposited on May 14, 1998 as ATCC 209861.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as  
30 DNA14007 comprising the nucleotide sequence of Figure 99 (SEQ ID NO:271).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA12733 comprising the nucleotide sequence of Figure 100 (SEQ ID NO:272).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA12746 comprising the nucleotide sequence of Figure 101 (SEQ ID NO:273).

35 In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA12834 comprising the nucleotide sequence of Figure 102 (SEQ ID NO:274).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA12846 comprising the nucleotide sequence of Figure 103 (SEQ ID NO:275).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA13104 comprising the nucleotide sequence of Figure 104 (SEQ ID NO:276).

5 In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA13259 comprising the nucleotide sequence of Figure 105 (SEQ ID NO:277).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA13959 comprising the nucleotide sequence of Figure 106 (SEQ ID NO:278).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA13961 comprising the nucleotide sequence of Figure 107 (SEQ ID NO:279).

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43. **PRO983**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to a vesicle associated protein, VAP-33, wherein the polypeptide is designated in the present application as "PRO983".

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO983 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO983 polypeptide having amino acid residues 1 to 243 of Figure 109 (SEQ ID NO:284), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO983 polypeptide having amino acid residue 1 to X of Figure 109 (SEQ ID NO:284) where X is any amino acid from  
20 219 to 228 of Figure 109 (SEQ ID NO:284), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA53977-1371 vector deposited on May 14, 1998 as ATCC 209862 which includes the nucleotide sequence encoding PRO983.

25 In another embodiment, the invention provides isolated PRO983 polypeptide. In particular, the invention provides isolated native sequence PRO983 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 243 of Figure 109 (SEQ ID NO:284). Additional embodiments of the present invention are directed to PRO983 polypeptides comprising amino acid 1 to X of Figure 109 (SEQ ID NO:284), where X is any amino acid from 219 to 228 of Figure 109 (SEQ ID NO:284). Optionally, the PRO983 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of  
30 the DNA53977-1371 vector deposited on May 14, 1998 as ATCC 209862.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA17130 comprising the nucleotide sequence of Figure 110 (SEQ ID NO:285).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA23466 comprising the nucleotide sequence of Figure 111 (SEQ ID NO:286).

35 In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA26818 comprising the nucleotide sequence of Figure 112 (SEQ ID NO:287).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA37618 comprising the nucleotide sequence of Figure 113 (SEQ ID NO:288).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA41732 comprising the nucleotide sequence of Figure 114 (SEQ ID NO:289).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as  
5 DNA45980 comprising the nucleotide sequence of Figure 115 (SEQ ID NO:290).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA46372 comprising the nucleotide sequence of Figure 116 (SEQ ID NO:291).

#### 44. PRO1057

10 Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to proteases, wherein the polypeptide is designated in the present application as "PRO1057".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1057 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1057 polypeptide having amino acid residues 1 to 413 of Figure 118 (SEQ ID NO:296), or is complementary to such  
15 encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1057 polypeptide having amino acid residues about 17 to 413 of Figure 118 (SEQ ID NO:296), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the  
20 DNA57253-1382 vector deposited on May 14, 1998 as ATCC 209867 which includes the nucleotide sequence encoding PRO1057.

In another embodiment, the invention provides isolated PRO1057 polypeptide. In particular, the invention provides isolated native sequence PRO1057 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 413 of Figure 118 (SEQ ID NO:296). Additional embodiments of the  
25 present invention are directed to PRO1057 polypeptides comprising amino acids about 17 to 413 of Figure 118 (SEQ ID NO:296). Optionally, the PRO1057 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA57253-1382 vector deposited on May 14, 1998 as ATCC 209867.

#### 30 45. PRO1071

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to thrombospondin, wherein the polypeptide is designated in the present application as "PRO1071".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1071 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1071  
35 polypeptide having amino acid residues 1 to 525 of Figure 120 (SEQ ID NO:301), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under



high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1071 polypeptide having amino acid residues about 26 to 525 of Figure 120 (SEQ ID NO:301), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA58847-1383 vector deposited on May 20, 1998 as ATCC 209879 which includes the nucleotide sequence encoding PRO1071.

In another embodiment, the invention provides isolated PRO1071 polypeptide. In particular, the invention provides isolated native sequence PRO1071 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 525 of Figure 120 (SEQ ID NO:301). Additional embodiments of the present invention are directed to PRO1071 polypeptides comprising amino acids about 26 to 525 of Figure 120 (SEQ ID NO:301). Optionally, the PRO1071 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA58847-1383 vector deposited on May 20, 1998 as ATCC 209879.

#### 46. PRO1072

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to reductase proteins, wherein the polypeptide is designated in the present application as "PRO1072".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1072 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1072 polypeptide having amino acid residues 1 to 336 of Figure 122 (SEQ ID NO:303), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1072 polypeptide having amino acid residues about 22 to 336 of Figure 122 (SEQ ID NO:303), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA58747-1384 vector deposited on May 14, 1998 as ATCC 209868 which includes the nucleotide sequence encoding PRO1072.

In another embodiment, the invention provides isolated PRO1072 polypeptide. In particular, the invention provides isolated native sequence PRO1072 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 336 of Figure 122 (SEQ ID NO:303). Additional embodiments of the present invention are directed to PRO1072 polypeptides comprising amino acids about 22 to 336 of Figure 122 (SEQ ID NO:303). Optionally, the PRO1072 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA58747-1384 vector deposited on May 14, 1998 as ATCC 209868.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA40210 comprising the nucleotide sequence of Figure 123 (SEQ ID NO:304).

**47. PRO1075**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to protein disulfide isomerase, wherein the polypeptide is designated in the present application as "PRO1075".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1075 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1075 polypeptide having amino acid residues 1 to 406 of Figure 125 (SEQ ID NO:309), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1075 polypeptide having amino acid residues about 30 to 406 of Figure 125 (SEQ ID NO:309), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA57689-1385 vector deposited on May 14, 1998 as ATCC 209869 which includes the nucleotide sequence encoding PRO1075.

In another embodiment, the invention provides isolated PRO1075 polypeptide. In particular, the invention provides isolated native sequence PRO1075 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 406 of Figure 125 (SEQ ID NO:309). Additional embodiments of the present invention are directed to PRO1075 polypeptides comprising amino acids about 30 to 406 of Figure 125 (SEQ ID NO:309). Optionally, the PRO1075 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA57689-1385 vector deposited on May 14, 1998 as ATCC 209869.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA13059 comprising the nucleotide sequence of Figure 126 (SEQ ID NO:310).

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA19463 comprising the nucleotide sequence of Figure 127 (SEQ ID NO:311).

**48. PRO181**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to the cornichon protein, wherein the polypeptide is designated in the present application as "PRO181".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO181 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO181 polypeptide having amino acid residues 1 to 144 of Figure 129 (SEQ ID NO:322), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO181 polypeptide having amino acid residues about 21 to 144 of Figure 129 (SEQ ID NO:322) or amino acid 1 or about 21 to X of Figure 129 (SEQ ID NO:322) where X is any amino acid from 52 to 61 of Figure 129 (SEQ ID NO:322), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may

comprise the cDNA insert of the DNA23330-1390 vector deposited on April 14, 1998 as ATCC 209775 which includes the nucleotide sequence encoding PRO181.

In another embodiment, the invention provides isolated PRO181 polypeptide. In particular, the invention provides isolated native sequence PRO181 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 144 of Figure 129 (SEQ ID NO:322). Additional embodiments of the present invention are directed to PRO181 polypeptides comprising amino acids about 21 to 144 of Figure 129 (SEQ ID NO:322) or amino acid 1 or about 21 to X of Figure 129 (SEQ ID NO:322), where X is any amino acid from 52 to 61 of Figure 129 (SEQ ID NO:322). Optionally, the PRO181 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA23330-1390 vector deposited on April 14, 1998 as ATCC 209775.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA13242 comprising the nucleotide sequence of Figure 130 (SEQ ID NO:323).

#### 49. PRO195

Applicants have identified a cDNA clone that encodes a novel transmembrane polypeptide, wherein the polypeptide is designated in the present application as "PRO195".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO195 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO195 polypeptide having amino acid residues 1 to 323 of Figure 132 (SEQ ID NO:330), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO195 polypeptide having amino acid residues about 32 to 323 of Figure 132 (SEQ ID NO:330) or amino acid 1 or about 32 to X of Figure 132 (SEQ ID NO:330) where X is any amino acid from 236 to 245 of Figure 132 (SEQ ID NO:330), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA26847-1395 vector deposited on April 14, 1998 as ATCC 209772 which includes the nucleotide sequence encoding PRO195.

In another embodiment, the invention provides isolated PRO195 polypeptide. In particular, the invention provides isolated native sequence PRO195 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 323 of Figure 132 (SEQ ID NO:330). Additional embodiments of the present invention are directed to PRO195 polypeptides comprising amino acids about 32 to 323 of Figure 132 (SEQ ID NO:330) or amino acid 1 or about 32 to X of Figure 132 (SEQ ID NO:330), where X is any amino acid from 236 to 245 of Figure 132 (SEQ ID NO:330). Optionally, the PRO195 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA26847-1395 vector deposited on April 14, 1998 as ATCC 209772.

In another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequence of Figure 133 (SEQ ID NO:331), herein designated DNA15062.

In another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequence of Figure 134 (SEQ ID NO:332), herein designated DNA13199.

50. **PRO865**

Applicants have identified a cDNA clone that encodes a novel secreted polypeptide, wherein the polypeptide is designated in the present application as "PRO865".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO865 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO865 polypeptide having amino acid residues 1 to 468 of Figure 136 (SEQ ID NO:337), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO865 polypeptide having amino acid residues about 24 to 229 of Figure 136 (SEQ ID NO:337), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA53974-1401 vector deposited on April 14, 1998 as ATCC 209774 which includes the nucleotide sequence encoding PRO865.

In another embodiment, the invention provides isolated PRO865 polypeptide. In particular, the invention provides isolated native sequence PRO865 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 468 of Figure 136 (SEQ ID NO:337). An additional embodiment of the present invention is directed to a PRO865 polypeptide comprising amino acids about 24 to 468 of Figure 136 (SEQ ID NO:337). Optionally, the PRO865 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA53974-1401 vector deposited on April 14, 1998 as ATCC 209774.

In another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequence of Figure 137 (SEQ ID NO:338), herein designated as DNA37642.

51. **PRO827**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to integrin proteins, wherein the polypeptide is designated in the present application as "PRO827".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO827 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO827 polypeptide having amino acid residues 1 to 124 of Figure 139 (SEQ ID NO:346), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO827 polypeptide having amino acid residues about 23 to 124 of Figure 139 (SEQ ID NO:346), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the

DNA57039-1402 vector deposited on April 14, 1998 as ATCC 209777 which includes the nucleotide sequence encoding PRO827.

In another embodiment, the invention provides isolated PRO827 polypeptide. In particular, the invention provides isolated native sequence PRO827 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 124 of Figure 139 (SEQ ID NO:346). An additional embodiment of the present invention is directed to a PRO827 polypeptide comprising amino acids about 23 to 124 of Figure 139 (SEQ ID NO:346). Optionally, the PRO827 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA57039-1402 vector deposited on April 14, 1998 as ATCC 209777.

10 52. **PRO1114**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to cytokine receptor family-4 proteins, wherein the polypeptide is designated in the present application as "PRO1114".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1114 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1114 polypeptide having amino acid residues 1 to 311 of Figure 142 (SEQ ID NO:352), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO1114 polypeptide having amino acid residues about 30 to 311 of Figure 142 (SEQ ID NO:352) or amino acid 1 or about 30 to X of Figure 142 (SEQ ID NO:352), where X is any amino acid from 225 to 234 of Figure 142 (SEQ ID NO:352), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA57033-1403 vector deposited on May 27, 1998 as ATCC 209905 which includes the nucleotide sequence encoding PRO1114.

In another embodiment, the invention provides isolated PRO1114 polypeptide. In particular, the invention provides isolated native sequence PRO1114 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 311 of Figure 142 (SEQ ID NO:352). Additional embodiments of the present invention are directed to PRO1114 polypeptides comprising amino acids about 30 to 311 of Figure 142 (SEQ ID NO:352) or amino acid 1 or about 30 to X of Figure 142 (SEQ ID NO:352), where X is any amino acid from 225 to 234 of Figure 142 (SEQ ID NO:352). Optionally, the PRO1114 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA57033-1403 vector deposited on May 27, 1998 as ATCC 209905.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA48466 comprising the nucleotide sequence of Figure 143 (SEQ ID NO:353).

A cDNA clone (DNA57033-1403) has been identified that encodes a novel interferon receptor polypeptide, designated in the present application as "PRO1114 interferon receptor".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

a PRO1114 interferon receptor polypeptide.

In one aspect, the isolated nucleic acid comprises DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO1114 interferon receptor polypeptide having the sequence of amino acid residues from about 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352), or (b) the complement of the DNA molecule of (a).

In another aspect, the invention concerns an isolated nucleic acid molecule encoding a PRO1114 interferon receptor polypeptide comprising DNA hybridizing to the complement of the nucleic acid between about nucleotides 250 or about 337 and about 1182, inclusive, of Figure 141 (SEQ ID NO:351). Preferably, hybridization occurs under stringent hybridization and wash conditions.

In a further aspect, the invention concerns an isolated nucleic acid molecule comprising DNA having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209905 (DNA57033-1403) or (b) the complement of the nucleic acid molecule of (a). In a preferred embodiment, the nucleic acid comprises a DNA encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209905 (DNA57033-1403).

In still a further aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352), or (b) the complement of the DNA of (a).

In a further aspect, the invention concerns an isolated nucleic acid molecule having at least 10 nucleotides and produced by hybridizing a test DNA molecule under stringent conditions with (a) a DNA molecule encoding a PRO1114 interferon receptor polypeptide having the sequence of amino acid residues from 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352), or (b) the complement of the DNA molecule of (a), and, if the DNA molecule has at least about an 80 % sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), isolating the test DNA molecule.

In a specific aspect, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1114 interferon receptor polypeptide, with or without the N-terminal signal sequence and/or the initiating methionine, and its soluble, i.e., transmembrane domain deleted or inactivated variants, or is complementary to such encoding nucleic acid molecule. The signal peptide has been tentatively identified as extending from about amino acid position 1 to about amino acid position 29 in the sequence of Figure 142 (SEQ ID NO:352). The transmembrane domain has been tentatively identified as extending from about amino acid position 230 to about amino acid position 255 in the PRO1114 interferon receptor amino acid sequence (Figure 142, SEQ ID NO:352).

In another aspect, the invention concerns an isolated nucleic acid molecule comprising (a) DNA encoding a polypeptide scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352), or (b) the complement of the DNA of (a).

5 Another embodiment is directed to fragments of a PRO1114 interferon receptor polypeptide coding sequence that may find use as hybridization probes. Such nucleic acid fragments are from about 20 to about 80 nucleotides in length, preferably from about 20 to about 60 nucleotides in length, more preferably from about 20 to about 50 nucleotides in length and most preferably from about 20 to about 40 nucleotides in length and may be derived from the nucleotide sequence shown in Figure 141 (SEQ ID NO:351).

10 In another embodiment, the invention provides a vector comprising DNA encoding PRO1114 interferon receptor or its variants. The vector may comprise any of the isolated nucleic acid molecules hereinabove identified.

A host cell comprising such a vector is also provided. By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing PRO1114 interferon receptor polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of PRO1114 interferon receptor and recovering PRO1114 interferon receptor from the cell culture.

In another embodiment, the invention provides isolated PRO1114 interferon receptor polypeptide encoded by any of the isolated nucleic acid sequences hereinabove identified.

20 In a specific aspect, the invention provides isolated native sequence PRO1114 interferon receptor polypeptide, which in certain embodiments, includes an amino acid sequence comprising residues 1 or about 30 to about 311 of Figure 142 (SEQ ID NO:352).

In another aspect, the invention concerns an isolated PRO1114 interferon receptor polypeptide comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to the sequence of amino acid residues 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352).

30 In a further aspect, the invention concerns an isolated PRO1114 interferon receptor polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352).

In yet another aspect, the invention concerns an isolated PRO1114 interferon receptor polypeptide, comprising the sequence of amino acid residues 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352), or a fragment thereof sufficient to provide a binding site for an anti-PRO1114 interferon receptor antibody. Preferably, the PRO1114 interferon receptor fragment retains a qualitative biological activity of a native PRO1114 interferon receptor polypeptide.

35 In a still further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA

molecule under stringent conditions with (a) a DNA molecule encoding a PRO1114 interferon receptor polypeptide having the sequence of amino acid residues from about 1 or about 30 to about 311, inclusive of Figure 142 (SEQ ID NO:352), or (b) the complement of the DNA molecule of (a), and if the test DNA molecule has at least about an 80% sequence identity, preferably at least about an 85% sequence identity, more preferably at least about a 90% sequence identity, most preferably at least about a 95% sequence identity to (a) or (b), (ii) 5 culturing a host cell comprising the test DNA molecule under conditions suitable for expression of the polypeptide, and (iii) recovering the polypeptide from the cell culture.

In another embodiment, the invention provides chimeric molecules comprising a PRO1114 interferon receptor polypeptide fused to a heterologous polypeptide or amino acid sequence. An example of such a chimeric molecule comprises a PRO1114 interferon receptor polypeptide fused to an epitope tag sequence or a 10 Fc region of an immunoglobulin.

In another embodiment, the invention provides an antibody which specifically binds to a PRO1114 interferon receptor polypeptide. Optionally, the antibody is a monoclonal antibody.

In yet another embodiment, the invention concerns agonists and antagonists of a native PRO1114 interferon receptor polypeptide. In a particular embodiment, the agonist or antagonist is an anti-PRO1114 15 interferon receptor antibody.

In a further embodiment, the invention concerns a method of identifying agonists or antagonists of a native PRO1114 interferon receptor polypeptide by contacting the native PRO1114 interferon receptor polypeptide with a candidate molecule and monitoring a biological activity mediated by said polypeptide.

In a still further embodiment, the invention concerns a composition comprising a PRO1114 interferon 20 receptor polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

### 53. PRO237

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to carbonic 25 anhydrase, wherein the polypeptide is designated in the present application as "PRO237".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO237 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO237 polypeptide having amino acid residues 1 to 328 of Figure 145 (SEQ ID NO:358), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under 30 high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO237 polypeptide having amino acid residues about 24 to 328 of Figure 145 (SEQ ID NO:358) or amino acid 1 or about 24 to X of Figure 145 (SEQ ID NO:358), where X is any amino acid from 172 to 181 of Figure 145 (SEQ ID NO:358), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may 35 comprise the cDNA insert of the DNA34353-1428 vector deposited on May 12, 1998 as ATCC 209855 which includes the nucleotide sequence encoding PRO237.



In another embodiment, the invention provides isolated PRO237 polypeptide. In particular, the invention provides isolated native sequence PRO237 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 328 of Figure 145 (SEQ ID NO:358). Additional embodiments of the present invention are directed to PRO237 polypeptides comprising amino acids about 24 to 328 of Figure 145 (SEQ ID NO:358) or amino acid 1 or about 24 to X of Figure 145 (SEQ ID NO:358), where X is any amino acid from 172 to 181 of Figure 145 (SEQ ID NO:358). Optionally, the PRO237 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA34353-1428 vector deposited on May 12, 1998 as ATCC 209855.

54. PRO541

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to a trypsin inhibitor protein, wherein the polypeptide is designated in the present application as "PRO541".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO541 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO541 polypeptide having amino acid residues 1 to 500 of Figure 147 (SEQ ID NO:363), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO541 polypeptide having amino acid residues about 21 to 500 of Figure 147 (SEQ ID NO:363), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA45417-1432 vector deposited on May 27, 1998 as ATCC 209910 which includes the nucleotide sequence encoding PRO541.

In another embodiment, the invention provides isolated PRO541 polypeptide. In particular, the invention provides isolated native sequence PRO541 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 500 of Figure 147 (SEQ ID NO:363). Additional embodiments of the present invention are directed to PRO541 polypeptides comprising amino acids about 21 to 500 of Figure 147 (SEQ ID NO:363). Optionally, the PRO541 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA45417-1432 vector deposited on May 27, 1998 as ATCC 209910.

55. PRO273

Applicants have identified a cDNA clone that encodes a novel polypeptide, wherein the polypeptide is designated in the present application as "PRO273".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO273 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO273 polypeptide having amino acid residues 1 through 111 of Figure 149 (SEQ ID NO:370), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally,

under high stringency conditions.

In another embodiment, the invention provides isolated PRO273 polypeptide. In particular, the invention provides isolated native sequence PRO273 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 111 of Figure 149 (SEQ ID NO:370).

5    56.    **PRO701**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to neuroligins 1, 2, and 3, wherein the polypeptide is designated in the present application as "PRO701".

10    In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO701 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO701 polypeptide having amino acid residues 1 through 816 of Figure 151 (SEQ ID NO:375), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited with the ATCC on March 31, 1998 which includes the nucleotide sequence encoding PRO701.

15    In another embodiment, the invention provides isolated PRO701 polypeptide. In particular, the invention provides isolated native sequence PRO701 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 816 of Figure 151 (SEQ ID NO:375). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO701 polypeptide. Optionally, the PRO701 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited with the ATCC on March 31, 1998.

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57.    **PRO704**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with VIP36, wherein the polypeptide is designated in the present application as "PRO704".

25    In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO704 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO704 polypeptide having amino acid residues 1 through 348 of Figure 153 (SEQ ID NO:380), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 31, 1998 with the ATCC as DNA50911-1288, which includes the nucleotide sequence encoding PRO704.

30    In another embodiment, the invention provides isolated PRO704 polypeptide. In particular, the invention provides isolated native sequence PRO704 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 348 of Figure 153 (SEQ ID NO:380). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO704 polypeptide. Optionally, the PRO704 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 31, 1998 with the ATCC as DNA50911-1288.

**58. PRO706**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to prostatic acid phosphatase precursor and lysosomal acid phosphatase precursor, wherein the polypeptide is designated in the present application as "PRO706".

5 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO706 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO706 polypeptide having amino acid residues 1 through 480 of Figure 155 (SEQ ID NO:385), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on April 21, 1998 with the ATCC as DNA48329-1290 which includes the nucleotide sequence  
10 encoding PRO706.

In another embodiment, the invention provides isolated PRO706 polypeptide. In particular, the invention provides isolated native sequence PRO706 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 480 of Figure 155 (SEQ ID NO:385), or comprising residues 19 through 480 of Figure 155 (SEQ ID NO:385). Optionally, the PRO706 polypeptide is obtained or is obtainable  
15 by expressing the polypeptide encoded by the cDNA insert of the vector deposited on April 21, 1998 with the ATCC as DNA48329-1290.

**59. PRO707**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to  
20 cadherins, particularly cadherin FIB3, wherein the polypeptide is designated in the present application as "PRO707".

~~In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding~~  
a PRO707 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO707 polypeptide having amino acid residues 1 to 916 of Figure 157 (SEQ ID NO:390), or is complementary to such  
25 encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 27, 1998 with the ATCC as DNA48306-1291 which includes the nucleotide sequence encoding PRO707.

In another embodiment, the invention provides isolated PRO707 polypeptide. In particular, the  
30 invention provides isolated native sequence PRO707 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 916 of Figure 157 (SEQ ID NO:390). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO707 polypeptide. Optionally, the PRO707 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 27, 1998 with the ATCC as DNA48306-1291.

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**60. PRO322**

Applicants have identified a cDNA clone that encodes a novel polypeptide having homology to neuropsin, wherein the polypeptide is designated in the present application as "PRO322".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO322 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO322 polypeptide having amino acid residues 1 or 24 through 260 of Figure 159 (SEQ ID NO:395), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 11, 1998 as ATCC no. 209669 which includes the nucleotide sequence encoding PRO322.

In another embodiment, the invention provides isolated PRO322 polypeptide. In particular, the invention provides isolated native sequence PRO322 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 or 24 through 260 of Figure 159 (SEQ ID NO:395). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO322 polypeptide. Optionally, the PRO322 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 11, 1998 as ATCC no. 209669.

**61. PRO526**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with ALS, wherein the polypeptide is designated in the present application as "PRO526".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO526 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO526 polypeptide having amino acid residues 1 to 473 of Figure 161 (SEQ ID NO:400), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 26, 1998 with the ATCC as DNA44184-1319 which includes the nucleotide sequence encoding PRO526.

In another embodiment, the invention provides isolated PRO526 polypeptide. In particular, the invention provides isolated native sequence PRO526 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 473 of Figure 161 (SEQ ID NO:400). Optionally, the PRO526 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 26, 1998 with the ATCC as DNA44184-1319 which includes the nucleotide sequence encoding PRO526.

**62. PRO531**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with protocadherins, wherein the polypeptide is designated in the present application as "PRO531".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO531 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO531 polypeptide having amino acid residues 1 to 789 of Figure 163 (SEQ ID NO:405), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 26, 1998 as DNA48314-1320 which includes the nucleotide sequence encoding PRO531.

In another embodiment, the invention provides isolated PRO531 polypeptide. In particular, the invention provides isolated native sequence PRO531 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 789 of Figure 163 (SEQ ID NO:405). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO531 polypeptide. Optionally, the PRO531 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 26, 1998 as DNA48314-1320.

### 63. PRO534

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with disulfide isomerase (sometimes referred to herein as protein disulfide isomerase), wherein the polypeptide is designated in the present application as "PRO534".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO534 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO534 polypeptide having amino acid residues 1 to 360 of Figure 165 (SEQ ID NO:410), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 26, 1998 as DNA48333-1321 which includes the nucleotide sequence encoding PRO534.

In another embodiment, the invention provides isolated PRO534 polypeptide. In particular, the invention provides isolated native sequence PRO534 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 360 of Figure 165 (SEQ ID NO:410). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO534 polypeptide. Optionally, the PRO534 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 26, 1998 as DNA48333-1321.

### 64. PRO697

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with sFRPs, wherein the polypeptide is designated in the present application as "PRO697".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO697 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO697 polypeptide having amino acid residues 1 through 295 of Figure 167 (SEQ ID NO:415), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally,

under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited with the ATCC on March 26, 1998 as DNA50920-1325 which includes the nucleotide sequence encoding PRO697.

In another embodiment, the invention provides isolated PRO697 polypeptide. In particular, the invention provides isolated native sequence PRO697 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 295 of Figure 167 (SEQ ID NO:415). Optionally, the PRO697 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited with the ATCC on March 26, 1998 as DNA50920-1325.

65. PRO717

Applicants have identified a cDNA clone that encodes a novel 12 transmembrane polypeptide, wherein the polypeptide is designated in the present application as "PRO717".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO717 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO717 polypeptide having amino acid residues 1 through 560 of Figure 169 (SEQ ID NO:420), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on April 28, 1998 with the ATCC as DNA50988-1326 which includes the nucleotide sequence encoding PRO717.

In another embodiment, the invention provides isolated PRO717 polypeptide. In particular, the invention provides isolated native sequence PRO717 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 560 of Figure 169 (SEQ ID NO:420). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO717 polypeptide. Optionally, the PRO717 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on April 28, 1998 with the ATCC as DNA50988-1326.

66. PRO731

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with protocadherin 4, wherein the polypeptide is designated in the present application as "PRO731".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO731 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO731 polypeptide having amino acid residues 1 through 1184 of Figure 171 (SEQ ID NO:425), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on March 31, 1998 with the ATCC as DNA48331-1329 which includes the nucleotide sequence encoding PRO731.

In another embodiment, the invention provides isolated PRO731 polypeptide. In particular, the

invention provides isolated native sequence PRO731 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 1184 of Figure 171 (SEQ ID NO:425). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO731 polypeptide. Optionally, the PRO731 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on March 31, 1998 with the ATCC as DNA48331-1329.

5

**67. PRO218**

Applicants have identified a cDNA clone that encodes a novel multi-transmembrane protein having sequence identity with membrane regulator proteins, wherein the polypeptide is designated in the present application as "PRO218".

10 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO218 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO218 polypeptide having amino acid residues 1 through 455 of Figure 173 (SEQ ID NO:430), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the  
15 vector deposited on April 28, 1998 with the ATCC as DNA30867-1335 which includes the nucleotide sequence encoding PRO218.

In another embodiment, the invention provides isolated PRO218 polypeptide. In particular, the invention provides isolated native sequence PRO218 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 455 of Figure 173 (SEQ ID NO:430). Optionally, the PRO218  
20 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on April 28, 1998 with the ATCC as DNA30867-1335.

~~In another embodiment, the invention provides an expressed sequence tag (EST) sequence comprising the nucleotide sequence of Figure 174 (SEQ ID NO:431), designated herein as DNA14472.~~

In another embodiment, the invention provides an expressed sequence tag (EST) sequence comprising  
25 the nucleotide sequence of Figure 175 (SEQ ID NO:432), designated herein as DNA15846.

**68. PRO768**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with integrins, wherein the polypeptide is designated in the present application as "PRO768".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO768 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO768 polypeptide having amino acid residues 1 through 1141 of Figure 177 (SEQ ID NO:437), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the  
35 vector deposited on April 6, 1998 as DNA55737-1345 which includes the nucleotide sequence encoding PRO768.

In another embodiment, the invention provides isolated PRO768 polypeptide. In particular, the invention provides isolated native sequence PRO768 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 1141 of Figure 177 (SEQ ID NO:437). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO768 polypeptide. Optionally, the PRO768 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on April 6, 1998 as DNA55737-1345.

69. **PRO771**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with testican, wherein the polypeptide is designated in the present application as "PRO771".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO771 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO771 polypeptide having amino acid residues 1 through 436 of Figure 179 (SEQ ID NO:442), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on April 7, 1998 with the ATCC as DNA49829-1346 which includes the nucleotide sequence encoding PRO771.

In another embodiment, the invention provides isolated PRO771 polypeptide. In particular, the invention provides isolated native sequence PRO771 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 436 of Figure 179 (SEQ ID NO:442). Optionally, the PRO771 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on April 7, 1998 with the ATCC as DNA49829-1346.

70. **PRO733**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with the T1/ST2 receptor binding protein, wherein the polypeptide is designated in the present application as "PRO733".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO733 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO733 polypeptide having amino acid residues 1 through 229 of Figure 181 (SEQ ID NO:447), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on April 7, 1998 with the ATCC as DNA52196-1348 which includes the nucleotide sequence encoding PRO733.

In another embodiment, the invention provides isolated PRO733 polypeptide. In particular, the invention provides isolated native sequence PRO733 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 229 of Figure 181 (SEQ ID NO:447). An additional embodiment



of the present invention is directed to an isolated extracellular domain of a PRO733 polypeptide. Optionally, the PRO733 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on April 7, 1998 as DNA52196-1348.

71. **PRO162**

5 Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with pancreatitis-associated protein, wherein the polypeptide is designated in the present application as "PRO162".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO162 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO162 polypeptide having amino acid residues 1 through 175 of Figure 183 (SEQ ID NO:452), or is complementary  
10 to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 6, 1998 with the ATCC as DNA56965-1356 which includes the nucleotide sequence encoding PRO162.

In another embodiment, the invention provides isolated PRO162 polypeptide. In particular, the  
15 invention provides isolated native sequence PRO162 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 175 of Figure 183 (SEQ ID NO:452). Optionally, the PRO162 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 6, 1998 with the ATCC as DNA56965-1356.

20 72. **PRO788**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with anti-neoplastic urinary protein, wherein the polypeptide is designated in the present application as "PRO788".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO788 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO788  
25 polypeptide having amino acid residues 1 through 125 of Figure 185 (SEQ ID NO:454), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 6, 1998 with the ATCC as DNA56405-1357 which includes the nucleotide sequence encoding PRO788.

In another embodiment, the invention provides isolated PRO788 polypeptide. In particular, the  
30 invention provides isolated native sequence PRO788 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 125 of Figure 185 (SEQ ID NO:454). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO788 polypeptide. Optionally, the PRO788 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert  
35 of the vector deposited on May 6, 1998 with the ATCC as DNA56405-1357.

**73. PRO1008**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with dickkopf-1 (dkk-1), wherein the polypeptide is designated in the present application as "PRO1008".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1008 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1008 polypeptide having amino acid residues 1 through 266 of Figure 187 (SEQ ID NO:456), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 20, 1998 with the ATCC as DNA57530-1375 which includes the nucleotide sequence encoding PRO1008.

In another embodiment, the invention provides isolated PRO1008 polypeptide. In particular, the invention provides isolated native sequence PRO1008 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 266 of Figure 187 (SEQ ID NO:456). Optionally, the PRO1008 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 20, 1998 with the ATCC as DNA57530-1375.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA16508 comprising the nucleotide sequence of Figure 188 (SEQ ID NO:457).

**74. PRO1012**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with disulfide isomerase and phospholipase C, wherein the polypeptide is designated in the present application as "PRO1012".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1012 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1012 polypeptide having amino acid residues 1 through 747 of Figure 190 (SEQ ID NO:459), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 14, 1998 with the ATCC as DNA56439-1376, which includes the nucleotide sequence encoding PRO1012.

In another embodiment, the invention provides isolated PRO1012 polypeptide. In particular, the invention provides isolated native sequence PRO1012 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 747 of Figure 190 (SEQ ID NO:459). Optionally, the PRO1012 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 14, 1998 with the ATCC as DNA56439-1376.

**75. PRO1014**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with reductase, wherein the polypeptide is designated in the present application as "PRO1014".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1014 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1014 polypeptide having amino acid residues 1 through 300 of Figure 192 (SEQ ID NO:464), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 20, 1998 as DNA56409-1377 with the ATCC which includes the nucleotide sequence encoding PRO1014.

In another embodiment, the invention provides isolated PRO1014 polypeptide. In particular, the invention provides isolated native sequence PRO1014 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 300 of Figure 192 (SEQ ID NO:464). Optionally, the PRO1014 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 20, 1998 as DNA56409-1377 with the ATCC.

**76. PRO1017**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with HNK-1 sulfotransferase, wherein the polypeptide is designated in the present application as "PRO1017".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1017 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1017 polypeptide having amino acid residues 1 through 414 of Figure 194 (SEQ ID NO:466), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 20, 1998 with the ATCC as DNA56112-1379 which includes the nucleotide sequence encoding PRO1017.

In another embodiment, the invention provides isolated PRO1017 polypeptide. In particular, the invention provides isolated native sequence PRO1017 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 414 of Figure 194 (SEQ ID NO:466). Optionally, the PRO1017 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 20, 1998 with the ATCC as DNA56112-1379.

**77. PRO474**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with dehydrogenase, wherein the polypeptide is designated in the present application as "PRO474".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO474 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO474

polypeptide having amino acid residues 1 through 270 of Figure 196 (SEQ ID NO:468), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 14, 1998 with the ATCC as DNA56045-1380 which includes the nucleotide sequence encoding PRO474.

5 In another embodiment, the invention provides isolated PRO474 polypeptide. In particular, the invention provides isolated native sequence PRO474 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 270 of Figure 196 (SEQ ID NO:468). Optionally, the PRO474 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 14, 1998 with the ATCC as DNA56045-1380.

10

78. **PRO1031**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with IL-17, wherein the polypeptide is designated in the present application as "PRO1031".

15 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1031 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1031 polypeptide having amino acid residues 1 through 180 of Figure 198 (SEQ ID NO:470), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 14, 1998 with the ATCC as DNA59294-1381 which includes the nucleotide sequence  
20 encoding PRO1031.

In another embodiment, the invention provides isolated PRO1031 polypeptide. In particular, the invention provides isolated native sequence PRO1031 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 180 of Figure 198 (SEQ ID NO:470). Optionally, the PRO1031 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector  
25 deposited on May 14, 1998 with the ATCC as DNA59294-1381.

79. **PRO938**

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity to protein disulfide isomerase, wherein the polypeptide is designated in the present application as "PRO938".

30 In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO938 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO938 polypeptide having amino acid residues 1 to 349 of Figure 200 (SEQ ID NO:472), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In other aspects, the isolated nucleic acid comprises DNA encoding the PRO938  
35 polypeptide having amino acid residues about 23 to 349 of Figure 200 (SEQ ID NO:472) or amino acid 1 or about 23 to X of Figure 200 (SEQ ID NO:472), where X is any amino acid from 186 to 195 of Figure 200 (SEQ

ID NO:472), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the DNA56433-1406 vector deposited on May 12, 1998, as ATCC Accession No. 209857 which includes the nucleotide sequence encoding PRO938.

In another embodiment, the invention provides isolated PRO938 polypeptide. In particular, the invention provides isolated native sequence PRO938 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 349 of Figure 200 (SEQ ID NO:472). Additional embodiments of the present invention are directed to PRO938 polypeptides comprising amino acids about 23 to 349 of Figure 200 (SEQ ID NO:472) or amino acid 1 or about 23 to X of Figure 200 (SEQ ID NO:472), where X is any amino acid from 186 to 195 of Figure 200 (SEQ ID NO:472). Optionally, the PRO938 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA56433-1406 vector deposited on May 12, 1998, as ATCC Accession No. 209857.

#### 80. PRO1082

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with a lectin-like oxidized LDL receptor, wherein the polypeptide is designated in the present application as "PRO1082".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO1082 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1082 polypeptide having amino acid residues 1 through 201 of Figure 202 (SEQ ID NO:477), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 14, 1998 with the ATCC as DNA53912-1457 which includes the nucleotide sequence encoding PRO1082.

In another embodiment, the invention provides isolated PRO1082 polypeptide. In particular, the invention provides isolated native sequence PRO1082 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 201 of Figure 202 (SEQ ID NO:477). An additional embodiment of the present invention is directed to an isolated domain of a PRO1082 polypeptide, excluding the transmembrane domain. Optionally, the PRO1082 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 14, 1998 with the ATCC as DNA53912-1457.

#### 81. PRO1083

Applicants have identified a cDNA clone that encodes a novel polypeptide having sequence identity with a TTM receptor, latrophilin-related protein 1, and a macrophage restricted cell surface glycoprotein, wherein the polypeptide is designated in the present application as "PRO1083".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding

a PRO1083 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO1083 polypeptide having amino acid residues 1 through 693 of Figure 204 (SEQ ID NO:483), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector deposited on May 12, 1998 with the ATCC as DNA50921-1458 which includes the nucleotide sequence encoding PRO1083.

In another embodiment, the invention provides isolated PRO1083 polypeptide. In particular, the invention provides isolated native sequence PRO1083 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 693 of Figure 204 (SEQ ID NO:483). An additional embodiment of the present invention is directed to an isolated extracellular domain of a PRO1083 polypeptide. Optionally, the PRO1083 polypeptide is obtained or is obtainable by expressing the polypeptide encoded by the cDNA insert of the vector deposited on May 12, 1998 with the ATCC as DNA50921-1458.

In another embodiment, the invention provides an expressed sequence tag (EST) designated herein as DNA24256 which comprises the nucleotide sequence of Figure 205 (SEQ ID NO:484).

## 82. PRO200

The objects of this invention, as defined generally supra, are achieved at least in part by the provision of a novel polypeptide, VEGF-E also herein designated PRO200, (SEQ ID NO:488) and the nucleic acid encoding therefor, SEQ ID NO:487, residues 259 through 1293.

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding a VEGF-E polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the VEGF-E polypeptide having amino acid residues 1 through 345 of Figure 207 (SEQ ID NO:488), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under low stringency conditions. In another embodiment, variants are provided wherein the VEGF-E nucleic acid has single or multiple deletions, substitutions, insertions, truncations or combinations thereof.

In another embodiment, the invention provides isolated VEGF-E polypeptide. In particular, the invention provides an isolated native sequence VEGF-E polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 through 345 of Figure 207 (SEQ ID NO:488). In another embodiment, variants are provided wherein the VEGF-E polypeptide has single or multiple deletions, substitutions, insertions, truncations or combinations thereof.

In yet further embodiments, the present invention is directed to compositions useful for treating indications where proliferation, survival and/or differentiation of cells is desired, comprising a therapeutically effective amount of a VEGF-E polypeptide hereof in admixture with a pharmaceutically acceptable carrier.

The invention further includes associated embodiments of VEGF-E such as modified VEGF-E polypeptides and modified variants which have the same biological applications as VEGF-E, and pharmaceutical compositions incorporating same. Inhibitors of VEGF-E are also provided.

**83. PRO285 and PRO286**

Applicants have identified two novel cDNA clones that encode novel human Toll polypeptides, designated in the present application as PRO285 (encoded by DNA40021-1154) and PRO286 (encoded by DNA42663-1154).

In one embodiment, the invention provides an isolated nucleic acid molecule comprising a DNA  
5 encoding a polypeptide having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO285 polypeptide having amino acid residues 27 to 839 of Figure 209 (SEQ ID NO:496); or (b) to a DNA molecule encoding a PRO286 polypeptide having amino acid residues 27 to 825 of Figure 211 (SEQ ID NO:498) or (c) the complement of the DNA molecule of (a) or (b). The  
10 complementary DNA molecule preferably remains stably bound to such encoding nucleic acid sequence under at least moderate, and optionally, under high stringency conditions.

In a further embodiment, the isolated nucleic acid molecule comprises a polynucleotide that has at least about 90%, preferably at least about 95% sequence identity with a polynucleotide encoding a polypeptide comprising the sequence of amino acids 1 to 839 of Figure 209 (SEQ ID NO:496); or at least about 90%,  
15 preferably at least about 95% sequence identity with a polynucleotide encoding a polypeptide comprising the sequence of amino acids 1 to 1041 of Figure 211 (SEQ ID NO:498).

In a specific embodiment, the invention provides an isolated nucleic acid molecule comprising DNA encoding native or variant PRO285 and PRO286 polypeptides, with or without the N-terminal signal sequence, and with or without the transmembrane regions of the respective full-length sequences. In one aspect, the  
20 isolated nucleic acid comprises DNA encoding a mature, full-length native PRO285 or PRO286 polypeptide having amino acid residues 1 to 1049 of Figure 209 (SEQ ID NO:496) and 1 to 1041 of Figure 211 (SEQ ID NO:498), or is complementary to such encoding nucleic acid sequence. In another aspect, the invention concerns an isolated nucleic acid molecule that comprises DNA encoding a native PRO285 or PRO286 polypeptide without an N-terminal signal sequence, or is complementary to such encoding nucleic acid sequence.  
25 In yet another embodiment, the invention concerns nucleic acid encoding transmembrane-domain deleted or inactivated forms of the full-length native PRO285 or PRO286 proteins.

In another embodiment, the invention the isolated nucleic acid molecule comprises the clone (DNA40021-1154) deposited on October 17, 1997, under ATCC number 209389; or the clone (DNA42663-1154) deposited on October 17, 1997, under ATCC number 209386.

30 In yet another embodiment, the invention provides a vector comprising DNA encoding PRO285 and PRO286 polypeptides, or their variants. Thus, the vector may comprise any of the isolated nucleic acid molecules hereinabove defined.

In another embodiment, the invention provides isolated PRO285 and PRO286 polypeptides. In particular, the invention provides isolated native sequence PRO285 and PRO286 polypeptides, which in one  
35 embodiment, include the amino acid sequences comprising residues 1 to 1049 and 1 to 1041 of Figures 209 and 211 (SEQ ID NOS:496 and 498), respectively. The invention also provides for variants of the PRO285 and

PRO286 polypeptides which are encoded by any of the isolated nucleic acid molecules hereinabove defined. Specific variants include, but are not limited to, deletion (truncated) variants of the full-length native sequence PRO285 and PRO286 polypeptides which lack the respective N-terminal signal sequences and/or have their respective transmembrane and/or cytoplasmic domains deleted or inactivated.

The invention also specifically includes antibodies with dual specificities, e.g., bispecific antibodies  
5 binding more than one Toll polypeptide.

In yet another embodiment, the invention concerns agonists and antagonists of the native PRO285 and PRO286 polypeptides. In a particular embodiment, the agonist or antagonist is an anti-PRO285 or anti-PRO286 antibody.

In a further embodiment, the invention concerns screening assays to identify agonists or antagonists of  
10 the native PRO285 and PRO286 polypeptides.

In a still further embodiment, the invention concerns a composition comprising a PRO285 or PRO286 polypeptide, or an agonist or antagonist as hereinabove defined, in combination with a pharmaceutically acceptable carrier.

The invention further concerns a composition comprising an antibody specifically binding a PRO285  
15 or PRO286 polypeptide, in combination with a pharmaceutically acceptable carrier.

The invention also concerns a method of treating septic shock comprising administering to a patient an effective amount of an antagonist of a PRO285 or PRO286 polypeptide. In a specific embodiment, the antagonist is a blocking antibody specifically binding a native PRO285 or PRO286 polypeptide.

20 **84. PRO213-1, PRO1330 and PRO1449**

The present invention concerns compositions and methods for the diagnosis and treatment of neoplastic cell growth and proliferation in mammals, including humans. The present invention is based on the identification of genes that are amplified in the genome of tumor cells. Such gene amplification is expected to be associated with the overexpression of the gene product and contribute to tumorigenesis. Accordingly, the proteins encoded  
25 by the amplified genes are believed to be useful targets for the diagnosis and/or treatment (including prevention) of certain cancers, and may act as predictors of the prognosis of tumor treatment.

In one embodiment, the present invention provides an isolated nucleic acid molecule comprising DNA encoding a PRO213-1, PRO1330 and/or PRO1449 polypeptide. In one aspect, the isolated nucleic acid comprises DNA encoding the PRO213-1, PRO1330 and/or PRO1449 polypeptide having amino acid residues 1 to 295 of Figure  
30 213 (SEQ ID NO:506), 20 to 273 of Figure 215 (SEQ ID NO:508) and 20 to 273 of Figure 217 (SEQ ID NO:510), respectively, or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. The isolated nucleic acid sequence may comprise the cDNA insert of the vector designated as DNA30943-1163 (ATCC 209791) deposited on April 21, 1998; DNA64907-1163-1 (ATCC 203242) deposited on September 9, 1998 and/or DNA64908-  
35 1163-1 (ATCC 203243) deposited on September 9, 1998.

In another embodiment, the present invention comprises an isolated nucleic acid molecule having at least



about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 90% sequence identity, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding a PRO213-1, PRO1330 and/or PRO1449 polypeptide having amino acid residues 1 to 295 of Figure 213 (SEQ ID NO:506), 20 to 273 of Figure 215 (SEQ ID NO:508) and 20 to 273 of Figure 217 (SEQ ID NO:510), respectively; or (b) the complement of the DNA molecule of (a).

5 In another embodiment, the invention provides an isolated PRO213-1, PRO1330 and/or PRO1449 polypeptide. In particular, the invention provides isolated native sequence PRO213-1, PRO1330 and/or PRO1449 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 295 of Figure 213 (SEQ ID NO:506), 20 to 273 of Figure 215 (SEQ ID NO:508) or 20 to 273 of Figure 217 (SEQ ID NO:510), respectively. Optionally, the PRO213-1, PRO1330 and/or PRO1449 polypeptide is obtained or  
10 obtainable by expressing the polypeptide encoded by the cDNA insert of the DNA30943-1163 (ATCC 209791), DNA64907-1163-1 (ATCC 203242) or DNA64908-1163-1 (ATCC 203243).

In another aspect, the invention provides an isolated PRO213-1, PRO1330, and/or PRO1449 polypeptide, comprising an amino acid sequence having at least about 80% sequence identity, preferably at least about 85% sequence identity, more preferably at least about 95% sequence identity to amino acid residues 1 to  
15 295 of Figure 213 (SEQ ID NO:506), 20 to 273 of Figure 215 (SEQ ID NO:508) or 20 to 273 of Figure 217 (SEQ ID NO:510), inclusive.

In yet another embodiment, the invention provides an isolated PRO213-1, PRO1330, and/or PRO1449 polypeptide, comprising the amino acid residues 1 to 295 of Figure 213 (SEQ ID NO:506), 20 to 273 of Figure 215 (SEQ ID NO:508) or 20 to 273 of Figure 217 (SEQ ID NO:510), or a fragment thereof sufficient to provide  
20 a binding site for an anti-PRO213-1, anti-PRO1330 and/or anti-PRO1449 antibody. Preferably, the PRO213-1, PRO1330, and/or PRO1449 fragment retains a qualitative biological activity of a native PRO213-1, PRO1330, and/or PRO1449 polypeptide.

In a further aspect, the invention concerns an isolated PRO213-1, PRO1330, and/or PRO1449 polypeptide, comprising an amino acid sequence scoring at least about 80% positives, preferably at least about  
25 85% positives, more preferably at least about 90% positives, most preferably at least about 95% positives when compared with the amino acid sequence of residues 1 to 295 of Figure 213 (SEQ ID NO:506), 20 to 273 of Figure 215 (SEQ ID NO:508) and 20 to 273 of Figure 217 (SEQ ID NO:510), respectively.

In still a further aspect, the invention provides a polypeptide produced by (i) hybridizing a test DNA molecule under stringent conditions with: (a) a DNA molecule encoding a PRO213-1, PRO1330, and/or  
30 PRO1449 polypeptide having the amino acid residues from 1 to 295 of Figure 213 (SEQ ID NO:506), 20 to 273 of Figure 215 (SEQ ID NO:508) and 20 to 273 of Figure 217 (SEQ ID NO:510), respectively; or the complement of the DNA molecule of (a), and if said test DNA molecule has at least about an 80% sequence identity to (a) or (b), (ii) culturing a host cell comprising said test DNA molecule under conditions suitable for the expression of said polypeptide, and (iii) recovering said polypeptide from the cell culture.

35 In one embodiment, the present invention concerns an isolated antibody which binds a PRO213-1, PRO1330 and/or PRO1449 polypeptide. In one aspect, the antibody induces death of a cell overexpressing a

PRO213-1, PRO1330 and/or PRO1449 polypeptide. In another aspect, the antibody is a monoclonal antibody, which preferably has nonhuman complementarity determining region (CDR) residues and human framework region (FR) residues. The antibody may be labeled and may be immobilized on a solid support. In a further aspect, the antibody is an antibody fragment, a single-chain antibody, or an anti-idiotypic antibody.

In another embodiment, the invention concerns a composition comprising an antibody which binds a  
5 PRO213-1, PRO1330 and/or PRO1449 polypeptide in admixture with a pharmaceutically acceptable carrier. In one aspect, the composition comprises a therapeutically effective amount of the antibody. In another aspect, the composition comprises a further active ingredient, which may, for example, be a further antibody or a cytotoxic or chemotherapeutic agent. Preferably, the composition is sterile.

In a further embodiment, the invention concerns nucleic acid encoding an anti-PRO213-1, anti-PRO1330  
10 and/or anti-PRO1449 antibody, and vectors and recombinant host cells comprising such nucleic acid.

The invention further concerns antagonists and agonists of a PRO213-1, PRO1330 and/or PRO1449 polypeptide that inhibit one or more of the functions or activities of the PRO213-1, PRO1330 and/or PRO1449 polypeptide.

In a further embodiment, the invention concerns isolated nucleic acid molecules that hybridize to the  
15 complement of the nucleic acid molecules encoding the PRO213-1, PRO1330 and/or PRO1449 polypeptides. The nucleic acid preferably is DNA, and hybridization preferably occurs under stringent conditions. Such nucleic acid molecules can act as antisense molecules of the amplified genes identified herein, which, in turn, can find use in the modulation of the respective amplified genes, or as antisense primers in amplification reactions. Furthermore, such sequences can be used as part of ribozyme and/or triple helix sequence which,  
20 in turn, may be used in regulation of the amplified genes.

In another embodiment, the invention concerns a method for determining the presence of a PRO213-1, PRO1330 and/or PRO1449 polypeptide comprising exposing a cell suspected of containing the PRO213-1, PRO1330 and/or PRO1449 polypeptide to an anti-PRO213-1, PRO1330 and/or PRO1449 antibody and determining binding of the antibody to the cell.

In yet another embodiment, the present invention concerns a method of diagnosing tumor in a mammal,  
25 comprising detecting the level of expression of a gene encoding a PRO213-1, PRO1330 and/or PRO1449 polypeptide (a) in a test sample of tissue cells obtained from the mammal, and (b) in a control sample of known normal tissue cells of the same cell type, wherein a higher expression level in the test sample indicates the presence of tumor in the mammal from which the test tissue cells were obtained.

In another embodiment, the present invention concerns a method of diagnosing tumor in a mammal,  
30 comprising (a) contacting an anti-PRO213-1, anti-PRO1330 and/or anti-PRO1449 antibody with a test sample of tissue cells obtained from the mammal, and (b) detecting the formation of a complex between the anti-PRO213-1, anti-PRO1330 and/or anti-PRO1449 antibody and the PRO213-1, PRO1330 and/or PRO1449 polypeptide in the test sample. The detection may be qualitative or quantitative, and may be performed in  
35 comparison with monitoring the complex formation in a control sample of known normal tissue cells of the same cell type. A larger quantity of complexes formed in the test sample indicates the presence of tumor in the

mammal from which the test tissue cells were obtained. The antibody preferably carries a detectable label. Complex formation can be monitored, for example, by light microscopy, flow cytometry, fluorimetry, or other techniques known in the art. The test sample is usually obtained from an individual suspected to have neoplastic cell growth or proliferation (e.g. cancerous cells).

In another embodiment, the present invention concerns a cancer diagnostic kit, comprising an anti-PRO213-1, anti-PRO1330 and/or anti-PRO1449 antibody and a carrier (e.g. a buffer) in suitable packaging. The kit preferably contains instructions for using the antibody to detect the PRO213-1, PRO1330 and/or PRO1449 polypeptide.

In yet another embodiment, the invention concerns a method for inhibiting the growth of tumor cells comprising exposing a cell which overexpresses a PRO213-1, PRO1330 and/or PRO1449 polypeptide to an effective amount of an agent inhibiting the expression and/or activity of the PRO213-1, PRO1330 and/or PRO1449 polypeptide. The agent preferably is an anti-PRO213-1, anti-PRO1330 and/or anti-PRO1449 antibody, a small organic and inorganic molecule, peptide, phosphopeptide, antisense or ribozyme molecule, or a triple helix molecule. In a specific aspect, the agent, e.g. anti-PRO213-1, anti-PRO1330 and/or anti-PRO1449 antibody induces cell death. In a further aspect, the tumor cells are further exposed to radiation treatment and/or a cytotoxic or chemotherapeutic agent.

In a further embodiment, the invention concerns an article of manufacture, comprising:

- a) a container;
- b) a label on the container; and
- c) a composition comprising an active agent contained within the container; wherein the composition is effective for inhibiting the growth of tumor cells, the label on the container indicates that the composition can be used for treating conditions characterized by overexpression of a PRO213-1, PRO1330 and/or PRO1449 polypeptide, and the active agent in the composition is an agent inhibiting the expression and/or activity of the PRO213-1, PRO1330 and/or PRO1449 polypeptide. In a preferred aspect, the active agent is an anti-PRO213-1, anti-PRO1330 and/or anti-PRO1449 antibody.

In yet a further embodiment, the invention provides a method for identifying a compound capable of inhibiting the expression and/or activity of a PRO213-1, PRO1330 and/or PRO1449 polypeptide, comprising contacting a candidate compound with a PRO213-1, PRO1330 and/or PRO1449 polypeptide under conditions and for a time sufficient to allow these two components to interact. In a specific aspect, either the candidate compound or the PRO213-1, PRO1330 and/or PRO1449 polypeptide is immobilized on a solid support. In another aspect, the non-immobilized component carries a detectable label.

#### 85. PRO298

Applicants have identified a cDNA clone that encodes a novel polypeptide. The DNA is designated in the present application as "DNA39975-1210", encoding a novel multi-transmembrane protein, referred to as "PRO298".

In one embodiment, the invention provides an isolated nucleic acid molecule comprising DNA having

at least about 80%, preferably at least about 85%, more preferably at least about 90%, most preferably at least about 95% sequence identity to (a) a DNA molecule encoding PRO298, comprising the sequence of amino acids 1 to 364 of Figure 219 (SEQ ID NO:515), or (b) the complement of the DNA molecule of (a). In one aspect, the isolated nucleic acid comprises DNA encoding a PRO298 polypeptide having amino acid residues 1 to 364 of Figure 219 (SEQ ID NO:515), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions.

In a further embodiment, the invention concerns an isolated nucleic acid molecule comprising DNA having at least an 80% sequence identity to (a) a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209783 (DNA39975-1210), or (b) the complement of the DNA molecule of (a).

In a still further embodiment, the invention concerns nucleic acid which comprises a DNA molecule encoding the same mature polypeptide encoded by the human protein cDNA in ATCC Deposit No. 209783 (DNA39975-1210).

In another embodiment, the invention provides isolated PRO298 polypeptide. In particular, the invention provides isolated native sequence PRO298 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 364 of Figure 219 (SEQ ID NO:515).

In another embodiment, the invention provides an expressed sequence tag (EST) designated DNA26832 comprising the nucleotide sequence of Figure 220 (SEQ ID NO:516).

#### 86. PRO337

Applicants have identified a cDNA clone (DNA43316-1237) that encodes a novel polypeptide, designated in the present application as "PRO337".

In one embodiment, the invention provides an isolated nucleic acid molecule having at least about 80% sequence identity to (a) a DNA molecule encoding a PRO337 polypeptide comprising the sequence of amino acids 1 to 344 of Figure 222 (SEQ ID NO:523), or (b) the complement of the DNA molecule of (a). The sequence identity preferably is about 85%, more preferably about 90%, most preferably about 95%. In one aspect, the isolated nucleic acid has at least about 80%, preferably at least about 85%, more preferably at least about 90%, and most preferably at least about 95 (including 96, 97, 98 and 99%) sequence identity with a polypeptide having amino acid residues 1 to 344 of Figure 222 (SEQ ID NO:523). Preferably, the highest degree of sequence identity occurs within the immunoglobulin and major histocompatibility domains (amino acids 113 to 130 of Figure 222, SEQ ID NO:523).

In a further embodiment, the isolated nucleic acid molecule comprises DNA encoding a neurotrimin polypeptide having amino acid residues 1 to 344 of Figure 222 (SEQ ID NO:523), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the invention provides a nucleic acid of the full length protein of clone DNA43316-1237, deposited with the ATCC under accession number ATCC 209487, alternatively the coding sequence of clone DNA43316-1237, deposited under accession number ATCC 209487.

In yet another embodiment, the invention provides isolated PRO337 polypeptide. In particular, the invention provides isolated native sequence PRO337 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 344 of Figure 222 (SEQ ID NO:523). Native PRO337 polypeptides with or without the native signal sequence (amino acids 1 to about 28 in Figure 222 (SEQ ID NO:523), and with or without the initiating methionine are specifically included. Alternatively, the invention provides a PRO337 polypeptide encoded by the nucleic acid deposited under accession number ATCC 209487.

In yet another embodiment, the invention provides an expressed sequence tag (EST) comprising the nucleotide sequences identified in Figure 223 as DNA42301 (SEQ ID NO:524).

#### 87. PRO403

Applicants have identified a cDNA clone (DNA55800-1263) that encodes a novel polypeptide, designated in the present application as "PRO403".

In one embodiment, the invention provides an isolated nucleic acid molecule having at least about 80% sequence identity to (a) a DNA molecule encoding a PRO403 polypeptide comprising the sequence of amino acids 1 to 736 of Figure 225 (SEQ ID NO:526), or (b) the complement of the DNA molecule of (a). The sequence identity preferably is about 85%, more preferably about 90%, most preferably about 95%. In one aspect, the isolated nucleic acid has at least about 80%, preferably at least about 85%, more preferably at least about 90%, and most preferably at least about 95% sequence identity with a polypeptide having amino acid residues 1 to 736 of Figure 225 (SEQ ID NO:526). Preferably, the highest degree of sequence identity occurs within: (1) the putative N-glycosylation sites (amino acid residues 132, 136, 177, 237, 282, 349, 505, 598 and 606; (2) Cys residues conserved with the Kell blood group protein family (amino acid residues 65, 70, 88 and 96) and the putative zinc binding motif (amino acid residues 570-579).

In a further embodiment, the isolated nucleic acid molecule comprises DNA encoding a PRO403 polypeptide having amino acid residues 1 to 736 of Figure 225 (SEQ ID NO:526), or is complementary to such encoding nucleic acid sequence, and remains stably bound to it under at least moderate, and optionally, under high stringency conditions. In another aspect, the invention provides a nucleic acid of the full length protein of clone DNA55800-1263, deposited with the ATCC under accession number ATCC 209680, alternatively the coding sequence of clone DNA55800-1263, deposited under accession number ATCC 209680.

In yet another embodiment, the invention provides isolated PRO403 polypeptide. In particular, the invention provides isolated native sequence PRO403 polypeptide, which in one embodiment, includes an amino acid sequence comprising residues 1 to 736 of Figure 225 (SEQ ID NO:526). Native PRO403 polypeptides with or the initiating methionine are specifically included. Alternatively, the invention provides a PRO403 polypeptide encoded by the nucleic acid deposited under accession number ATCC 209680.

In yet another embodiment, the invention provides an expressed sequence tag (EST) and other sequence fragments comprising the nucleotide sequences identified herein as DNA34415 (Figures 226A-B; SEQ ID NO:527); DNA49830 (Figure 227 ; SEQ ID NO:528) and DNA49831 (Figure 228; SEQ ID NO:529).

**88. Additional Embodiments**

In other embodiments of the present invention, the invention provides vectors comprising DNA encoding any of the above or below described polypeptides. A host cell comprising any such vector is also provided. By way of example, the host cells may be CHO cells, *E. coli*, or yeast. A process for producing any of the above or below described polypeptides is further provided and comprises culturing host cells under conditions suitable for expression of the desired polypeptide and recovering the desired polypeptide from the cell culture.

In other embodiments, the invention provides chimeric molecules comprising any of the above or below described polypeptides fused to a heterologous polypeptide or amino acid sequence. An example of such a chimeric molecule comprises any of the above or below described polypeptides fused to an epitope tag sequence or a Fc region of an immunoglobulin.

In another embodiment, the invention provides an antibody which specifically binds to any of the above or below described polypeptides. Optionally, the antibody is a monoclonal antibody.

In yet other embodiments, the invention provides oligonucleotide probes useful for isolating genomic and cDNA nucleotide sequences, wherein those probes may be derived from any of the above or below described nucleotide sequences.

**BRIEF DESCRIPTION OF THE DRAWINGS**

Figure 1 shows a nucleotide sequence (SEQ ID NO:1) of a native sequence PRO213 cDNA, wherein SEQ ID NO:1 is a clone designated herein as "UNQ187" and/or "DNA30943-1163".

Figure 2 shows the amino acid sequence (SEQ ID NO:2) derived from the coding sequence of SEQ ID NO:1 shown in Figure 1.

Figure 3 shows a nucleotide sequence (SEQ ID NO:6) of a native sequence PRO274 cDNA, wherein SEQ ID NO:6 is a clone designated herein as "UNQ241" and/or "DNA39987-1184".

Figure 4 shows the amino acid sequence (SEQ ID NO:7) derived from the coding sequence of SEQ ID NO:6 shown in Figure 3.

Figure 5 shows an EST nucleotide sequence designated herein as DNA17873 (SEQ ID NO:8).

Figure 6 shows an EST nucleotide sequence designated herein as DNA36157 (SEQ ID NO:9).

Figure 7 shows an EST nucleotide sequence designated herein as DNA28929 (SEQ ID NO:10).

Figure 8 shows a nucleotide sequence (SEQ ID NO:18) of a native sequence PRO300 cDNA, wherein SEQ ID NO:18 is a clone designated herein as "UNQ263" and/or "DNA40625-1189".

Figure 9 shows the amino acid sequence (SEQ ID NO:19) derived from the coding sequence of SEQ ID NO:18 shown in Figure 8.

Figure 10 shows a nucleotide sequence (SEQ ID NO:27) of a native sequence PRO284 cDNA, wherein SEQ ID NO:27 is a clone designated herein as "UNQ247" and/or "DNA23318-1211".

Figure 11 shows the amino acid sequence (SEQ ID NO:28) derived from the coding sequence of SEQ ID NO:27 shown in Figure 10.

Figure 12 shows an EST nucleotide sequence designated herein as DNA12982 (SEQ ID NO:29).

Figure 13 shows an EST nucleotide sequence designated herein as DNA15886 (SEQ ID NO:30).

Figure 14 shows a nucleotide sequence (SEQ ID NO:35) of a native sequence PRO296 cDNA, wherein SEQ ID NO:35 is a clone designated herein as "UNQ260" and/or "DNA39979-1213".

5 Figure 15 shows the amino acid sequence (SEQ ID NO:36) derived from the coding sequence of SEQ ID NO:35 shown in Figure 14.

Figure 16 shows an EST nucleotide sequence designated herein as DNA23020 (SEQ ID NO:37).

Figure 17 shows an EST nucleotide sequence designated herein as DNA21971 (SEQ ID NO:38).

Figure 18 shows an EST nucleotide sequence designated herein as DNA29037 (SEQ ID NO:39).

10 Figure 19 shows a nucleotide sequence (SEQ ID NO:44) of a native sequence PRO329 cDNA, wherein SEQ ID NO:44 is a clone designated herein as "UNQ291" and/or "DNA40594-1233".

Figure 20 shows the amino acid sequence (SEQ ID NO:45) derived from the coding sequence of SEQ ID NO:44 shown in Figure 19.

Figure 21 shows a nucleotide sequence (SEQ ID NO:51) of a native sequence PRO362 cDNA, wherein SEQ ID NO:51 is a clone designated herein as "UNQ317" and/or "DNA45416-1251".

15 Figure 22 shows the amino acid sequence (SEQ ID NO:52) derived from the coding sequence of SEQ ID NO:51 shown in Figure 21.

Figure 23 shows a nucleotide sequence (SEQ ID NO:58) of a native sequence PRO363 cDNA, wherein SEQ ID NO:58 is a clone designated herein as "UNQ318" and/or "DNA45419-1252".

20 Figure 24 shows the amino acid sequence (SEQ ID NO:59) derived from the coding sequence of SEQ ID NO:58 shown in Figure 23.

Figure 25 shows a nucleotide sequence (SEQ ID NO:63) of a native sequence PRO868 cDNA, wherein SEQ ID NO:63 is a clone designated herein as "UNQ437" and/or "DNA52594-1270".

Figure 26 shows the amino acid sequence (SEQ ID NO:64) derived from the coding sequence of SEQ ID NO:63 shown in Figure 25.

25 Figure 27 shows a nucleotide sequence (SEQ ID NO:68) of a native sequence PRO382 cDNA, wherein SEQ ID NO:68 is a clone designated herein as "UNQ323" and/or "DNA45234-1277".

Figure 28 shows the amino acid sequence (SEQ ID NO:69) derived from the coding sequence of SEQ ID NO:68 shown in Figure 27.

30 Figure 29 shows a nucleotide sequence (SEQ ID NO:73) of a native sequence PRO545 cDNA, wherein SEQ ID NO:73 is a clone designated herein as "UNQ346" and/or "DNA49624-1279".

Figure 30 shows the amino acid sequence (SEQ ID NO:74) derived from the coding sequence of SEQ ID NO:73 shown in Figure 29.

Figure 31 shows an EST nucleotide sequence designated herein as DNA13217 (SEQ ID NO:75).

35 Figure 32 shows a nucleotide sequence (SEQ ID NO:84) of a native sequence PRO617 cDNA, wherein SEQ ID NO:84 is a clone designated herein as "UNQ353" and/or "DNA48309-1280".

Figure 33 shows the amino acid sequence (SEQ ID NO:85) derived from the coding sequence of SEQ

ID NO:84 shown in Figure 32.

Figure 34 shows a nucleotide sequence (SEQ ID NO:89) of a native sequence PRO700 cDNA, wherein SEQ ID NO:89 is a clone designated herein as "UNQ364" and/or "DNA46776-1284".

Figure 35 shows the amino acid sequence (SEQ ID NO:90) derived from the coding sequence of SEQ ID NO:89 shown in Figure 34.

5 Figure 36 shows a nucleotide sequence (SEQ ID NO:96) of a native sequence PRO702 cDNA, wherein SEQ ID NO:96 is a clone designated herein as "UNQ366" and/or "DNA50980-1286".

Figure 37 shows the amino acid sequence (SEQ ID NO:97) derived from the coding sequence of SEQ ID NO:96 shown in Figure 36.

10 Figure 38 shows a nucleotide sequence (SEQ ID NO:101) of a native sequence PRO703 cDNA, wherein SEQ ID NO:101 is a clone designated herein as "UNQ367" and/or "DNA50913-1287".

Figure 39 shows the amino acid sequence (SEQ ID NO:102) derived from the coding sequence of SEQ ID NO:101 shown in Figure 38.

Figure 40 shows a nucleotide sequence (SEQ ID NO:108) of a native sequence PRO705 cDNA, wherein SEQ ID NO:108 is a clone designated herein as "UNQ369" and/or "DNA50914-1289".

15 Figure 41 shows the amino acid sequence (SEQ ID NO:109) derived from the coding sequence of SEQ ID NO:108 shown in Figure 40.

Figures 42A-B show a nucleotide sequence (SEQ ID NO:113) of a native sequence PRO708 cDNA, wherein SEQ ID NO:113 is a clone designated herein as "UNQ372" and/or "DNA48296-1292".

20 Figure 43 shows the amino acid sequence (SEQ ID NO:114) derived from the coding sequence of SEQ ID NO:113 shown in Figures 42A-B.

Figure 44 shows a nucleotide sequence (SEQ ID NO:118) of a native sequence PRO320 cDNA, wherein SEQ ID NO:118 is a clone designated herein as "UNQ281" and/or "DNA32284-1307".

Figure 45 shows the amino acid sequence (SEQ ID NO:119) derived from the coding sequence of SEQ ID NO:118 shown in Figure 44.

25 Figure 46 shows a nucleotide sequence (SEQ ID NO:123) of a native sequence PRO324 cDNA, wherein SEQ ID NO:123 is a clone designated herein as "UNQ285" and/or "DNA36343-1310".

Figure 47 shows the amino acid sequence (SEQ ID NO:124) derived from the coding sequence of SEQ ID NO:123 shown in Figure 46.

30 Figure 48 shows a nucleotide sequence (SEQ ID NO:131) of a native sequence PRO351 cDNA, wherein SEQ ID NO:131 is a clone designated herein as "UNQ308" and/or "DNA40571-1315".

Figure 49 shows the amino acid sequence (SEQ ID NO:132) derived from the coding sequence of SEQ ID NO:131 shown in Figure 48.

Figure 50 shows a nucleotide sequence (SEQ ID NO:136) of a native sequence PRO352 cDNA, wherein SEQ ID NO:136 is a clone designated herein as "UNQ309" and/or "DNA41386-1316".

35 Figure 51 shows the amino acid sequence (SEQ ID NO:137) derived from the coding sequence of SEQ ID NO:136 shown in Figure 50.



Figure 52 shows a nucleotide sequence (SEQ ID NO:144) of a native sequence PRO381 cDNA, wherein SEQ ID NO:144 is a clone designated herein as "UNQ322" and/or "DNA44194-1317".

Figure 53 shows the amino acid sequence (SEQ ID NO:145) derived from the coding sequence of SEQ ID NO:144 shown in Figure 52.

Figure 54 shows a nucleotide sequence (SEQ ID NO:149) of a native sequence PRO386 cDNA, wherein  
5 SEQ ID NO:149 is a clone designated herein as "UNQ326" and/or "DNA45415-1318".

Figure 55 shows the amino acid sequence (SEQ ID NO:150) derived from the coding sequence of SEQ ID NO:149 shown in Figure 54.

Figure 56 shows an EST nucleotide sequence designated herein as DNA23350 (SEQ ID NO:151).

Figure 57 shows an EST nucleotide sequence designated herein as DNA23536 (SEQ ID NO:152).

10 Figure 58 shows a nucleotide sequence (SEQ ID NO:156) of a native sequence PRO540 cDNA, wherein SEQ ID NO:156 is a clone designated herein as "UNQ341" and/or "DNA44189-1322".

Figure 59 shows the amino acid sequence (SEQ ID NO:157) derived from the coding sequence of SEQ ID NO:156 shown in Figure 58.

Figure 60 shows a nucleotide sequence (SEQ ID NO:161) of a native sequence PRO615 cDNA, wherein  
15 SEQ ID NO:161 is a clone designated herein as "UNQ352" and/or "DNA48304-1323".

Figure 61 shows the amino acid sequence (SEQ ID NO:162) derived from the coding sequence of SEQ ID NO:161 shown in Figure 60.

Figure 62 shows a nucleotide sequence (SEQ ID NO:168) of a native sequence PRO618 cDNA, wherein SEQ ID NO:168 is a clone designated herein as "UNQ354" and/or "DNA49152-1324".

20 Figure 63 shows the amino acid sequence (SEQ ID NO:169) derived from the coding sequence of SEQ ID NO:168 shown in Figure 62.

Figure 64 shows an EST nucleotide sequence designated herein as DNA25597 (SEQ ID NO:170).

Figure 65 shows a nucleotide sequence (SEQ ID NO:177) of a native sequence PRO719 cDNA, wherein SEQ ID NO:177 is a clone designated herein as "UNQ387" and/or "DNA49646-1327".

25 Figure 66 shows the amino acid sequence (SEQ ID NO:178) derived from the coding sequence of SEQ ID NO:177 shown in Figure 65.

Figure 67 shows a nucleotide sequence (SEQ ID NO:182) of a native sequence PRO724 cDNA, wherein SEQ ID NO:182 is a clone designated herein as "UNQ389" and/or "DNA49631-1328".

30 Figure 68 shows the amino acid sequence (SEQ ID NO:183) derived from the coding sequence of SEQ ID NO:182 shown in Figure 67.

Figure 69 shows a nucleotide sequence (SEQ ID NO:189) of a native sequence PRO772 cDNA, wherein SEQ ID NO:189 is a clone designated herein as "UNQ410" and/or "DNA49645-1347".

Figure 70 shows the amino acid sequence (SEQ ID NO:190) derived from the coding sequence of SEQ ID NO:189 shown in Figure 69.

35 Figure 71 shows an EST nucleotide sequence designated herein as DNA43509 (SEQ ID NO:191).

Figure 72 shows a nucleotide sequence (SEQ ID NO:195) of a native sequence PRO852 cDNA, wherein

SEQ ID NO:195 is a clone designated herein as "UNQ418" and/or "DNA45493-1349".

Figure 73 shows the amino acid sequence (SEQ ID NO:196) derived from the coding sequence of SEQ ID NO:195 shown in Figure 72.

Figure 74 shows a nucleotide sequence (SEQ ID NO:205) of a native sequence PRO853 cDNA, wherein SEQ ID NO:205 is a clone designated herein as "UNQ419" and/or "DNA48227-1350".

5        Figure 75 shows the amino acid sequence (SEQ ID NO:206) derived from the coding sequence of SEQ ID NO:205 shown in Figure 74.

Figures 76A-B show a nucleotide sequence (SEQ ID NO:210) of a native sequence PRO860 cDNA, wherein SEQ ID NO:210 is a clone designated herein as "UNQ421" and/or "DNA41404-1352".

10       Figure 77 shows the amino acid sequence (SEQ ID NO:211) derived from the coding sequence of SEQ ID NO:210 shown in Figures 76A-B.

Figure 78 shows a nucleotide sequence (SEQ ID NO:215) of a native sequence PRO846 cDNA, wherein SEQ ID NO:215 is a clone designated herein as "UNQ422" and/or "DNA44196-1353".

Figure 79 shows the amino acid sequence (SEQ ID NO:216) derived from the coding sequence of SEQ ID NO:215 shown in Figure 78.

15       Figure 80 shows a nucleotide sequence (SEQ ID NO:220) of a native sequence PRO862 cDNA, wherein SEQ ID NO:220 is a clone designated herein as "UNQ424" and/or "DNA52187-1354".

Figure 81 shows the amino acid sequence (SEQ ID NO:221) derived from the coding sequence of SEQ ID NO:220 shown in Figure 80.

20       Figure 82 shows a nucleotide sequence (SEQ ID NO:225) of a native sequence PRO864 cDNA, wherein SEQ ID NO:225 is a clone designated herein as "UNQ426" and/or "DNA48328-1355".

Figure 83 shows the amino acid sequence (SEQ ID NO:226) derived from the coding sequence of SEQ ID NO:225 shown in Figure 82.

Figure 84 shows a nucleotide sequence (SEQ ID NO:230) of a native sequence PRO792 cDNA, wherein SEQ ID NO:230 is a clone designated herein as "UNQ431" and/or "DNA56352-1358".

25       Figure 85 shows the amino acid sequence (SEQ ID NO:231) derived from the coding sequence of SEQ ID NO:230 shown in Figure 84.

Figure 86 shows a nucleotide sequence (SEQ ID NO:235) of a native sequence PRO866 cDNA, wherein SEQ ID NO:235 is a clone designated herein as "UNQ435" and/or "DNA53971-1359".

30       Figure 87 shows the amino acid sequence (SEQ ID NO:236) derived from the coding sequence of SEQ ID NO:235 shown in Figure 86.

Figure 88 shows a nucleotide sequence (SEQ ID NO:244) of a native sequence PRO871 cDNA, wherein SEQ ID NO:244 is a clone designated herein as "UNQ438" and/or "DNA50919-1361".

Figure 89 shows the amino acid sequence (SEQ ID NO:245) derived from the coding sequence of SEQ ID NO:244 shown in Figure 88.

35       Figure 90 shows a nucleotide sequence (SEQ ID NO:253) of a native sequence PRO873 cDNA, wherein SEQ ID NO:253 is a clone designated herein as "UNQ440" and/or "DNA44179-1362".

Figure 91 shows the amino acid sequence (SEQ ID NO:254) derived from the coding sequence of SEQ ID NO:253 shown in Figure 90.

Figure 92 shows a nucleotide sequence (SEQ ID NO:258) of a native sequence PRO940 cDNA, wherein SEQ ID NO:258 is a clone designated herein as "UNQ477" and/or "DNA54002-1367".

Figure 93 shows the amino acid sequence (SEQ ID NO:259) derived from the coding sequence of SEQ ID NO:258 shown in Figure 92.

Figure 94 shows a nucleotide sequence (SEQ ID NO:263) of a native sequence PRO941 cDNA, wherein SEQ ID NO:263 is a clone designated herein as "UNQ478" and/or "DNA53906-1368".

Figure 95 shows the amino acid sequence (SEQ ID NO:264) derived from the coding sequence of SEQ ID NO:263 shown in Figure 94.

Figure 96 shows an EST nucleotide sequence designated herein as DNA6415 (SEQ ID NO:265).

Figure 97 shows a nucleotide sequence (SEQ ID NO:269) of a native sequence PRO944 cDNA, wherein SEQ ID NO:269 is a clone designated herein as "UNQ481" and/or "DNA52185-1370".

Figure 98 shows the amino acid sequence (SEQ ID NO:270) derived from the coding sequence of SEQ ID NO:269 shown in Figure 97.

Figure 99 shows an EST nucleotide sequence designated herein as DNA14007 (SEQ ID NO:271).

Figure 100 shows an EST nucleotide sequence designated herein as DNA12773 (SEQ ID NO:272).

Figure 101 shows an EST nucleotide sequence designated herein as DNA12746 (SEQ ID NO:273).

Figure 102 shows an EST nucleotide sequence designated herein as DNA12834 (SEQ ID NO:274).

Figure 103 shows an EST nucleotide sequence designated herein as DNA12846 (SEQ ID NO:275).

Figure 104 shows an EST nucleotide sequence designated herein as DNA13104 (SEQ ID NO:276).

Figure 105 shows an EST nucleotide sequence designated herein as DNA13259 (SEQ ID NO:277).

Figure 106 shows an EST nucleotide sequence designated herein as DNA13959 (SEQ ID NO:278).

Figure 107 shows an EST nucleotide sequence designated herein as DNA13961 (SEQ ID NO:279).

Figure 108 shows a nucleotide sequence (SEQ ID NO:283) of a native sequence PRO983 cDNA, wherein SEQ ID NO:283 is a clone designated herein as "UNQ484" and/or "DNA53977-1371".

Figure 109 shows the amino acid sequence (SEQ ID NO:284) derived from the coding sequence of SEQ ID NO:283 shown in Figure 108.

Figure 110 shows an EST nucleotide sequence designated herein as DNA17130 (SEQ ID NO:285).

Figure 111 shows an EST nucleotide sequence designated herein as DNA23466 (SEQ ID NO:286).

Figure 112 shows an EST nucleotide sequence designated herein as DNA26818 (SEQ ID NO:287).

Figure 113 shows an EST nucleotide sequence designated herein as DNA37618 (SEQ ID NO:288).

Figure 114 shows an EST nucleotide sequence designated herein as DNA41732 (SEQ ID NO:289).

Figure 115 shows an EST nucleotide sequence designated herein as DNA45980 (SEQ ID NO:290).

Figure 116 shows an EST nucleotide sequence designated herein as DNA46372 (SEQ ID NO:291).

Figure 117 shows a nucleotide sequence (SEQ ID NO:295) of a native sequence PRO1057 cDNA, wherein SEQ ID NO:295 is a clone designated herein as "UNQ522" and/or "DNA57253-1382".

Figure 118 shows the amino acid sequence (SEQ ID NO:296) derived from the coding sequence of SEQ ID NO:295 shown in Figure 117.

Figure 119 shows a nucleotide sequence (SEQ ID NO:300) of a native sequence PRO1071 cDNA, wherein SEQ ID NO:300 is a clone designated herein as "UNQ528" and/or "DNA58847-1383".

5 Figure 120 shows the amino acid sequence (SEQ ID NO:301) derived from the coding sequence of SEQ ID NO:300 shown in Figure 119.

Figure 121 shows a nucleotide sequence (SEQ ID NO:302) of a native sequence PRO1072 cDNA, wherein SEQ ID NO:302 is a clone designated herein as "UNQ529" and/or "DNA58747-1384".

Figure 122 shows the amino acid sequence (SEQ ID NO:303) derived from the coding sequence of SEQ ID NO:302 shown in Figure 121.

10 Figure 123 shows an EST nucleotide sequence designated herein as DNA40210 (SEQ ID NO:304).

Figure 124 shows a nucleotide sequence (SEQ ID NO:308) of a native sequence PRO1075 cDNA, wherein SEQ ID NO:308 is a clone designated herein as "UNQ532" and/or "DNA57689-1385".

Figure 125 shows the amino acid sequence (SEQ ID NO:309) derived from the coding sequence of SEQ ID NO:308 shown in Figure 124.

15 Figure 126 shows an EST nucleotide sequence designated herein as DNA13059 (SEQ ID NO:310).

Figure 127 shows an EST nucleotide sequence designated herein as DNA19463 (SEQ ID NO:311).

Figure 128 shows a nucleotide sequence (SEQ ID NO:321) of a native sequence PRO181 cDNA, wherein SEQ ID NO:321 is a clone designated herein as "UNQ155" and/or "DNA23330-1390".

20 Figure 129 shows the amino acid sequence (SEQ ID NO:322) derived from the coding sequence of SEQ ID NO:321 shown in Figure 128.

Figure 130 shows an EST nucleotide sequence designated herein as DNA13242 (SEQ ID NO:323).

~~Figure 131 shows a nucleotide sequence (SEQ ID NO:329) of a native sequence PRO195 cDNA,~~  
wherein SEQ ID NO:329 is a clone designated herein as "UNQ169" and/or "DNA26847-1395".

25 Figure 132 shows the amino acid sequence (SEQ ID NO:330) derived from the coding sequence of SEQ ID NO:329 shown in Figure 131.

Figure 133 shows an EST nucleotide sequence designated herein as DNA15062 (SEQ ID NO:331).

Figure 134 shows an EST nucleotide sequence designated herein as DNA13199 (SEQ ID NO:332).

Figure 135 shows a nucleotide sequence (SEQ ID NO:336) of a native sequence PRO865 cDNA, wherein SEQ ID NO:336 is a clone designated herein as "UNQ434" and/or "DNA53974-1401".

30 Figure 136 shows the amino acid sequence (SEQ ID NO:337) derived from the coding sequence of SEQ ID NO:336 shown in Figure 135.

Figure 137 shows an EST nucleotide sequence designated herein as DNA37642 (SEQ ID NO:338).

Figure 138 shows a nucleotide sequence (SEQ ID NO:345) of a native sequence PRO827 cDNA, wherein SEQ ID NO:345 is a clone designated herein as "UNQ468" and/or "DNA57039-1402".

35 Figure 139 shows the amino acid sequence (SEQ ID NO:346) derived from the coding sequence of SEQ ID NO:345 shown in Figure 138.

Figure 140 shows an EST nucleotide sequence designated herein as DNA47751 (SEQ ID NO:347).

Figure 141 shows a nucleotide sequence (SEQ ID NO:351) of a native sequence PRO1114 cDNA, wherein SEQ ID NO:351 is a clone designated herein as "UNQ557" and/or "DNA57033-1403".

Figure 142 shows the amino acid sequence (SEQ ID NO:352) derived from the coding sequence of SEQ ID NO:351 shown in Figure 141.

5 Figure 143 shows an EST nucleotide sequence designated herein as DNA48466 (SEQ ID NO:353).

Figure 144 shows a nucleotide sequence (SEQ ID NO:357) of a native sequence PRO237 cDNA, wherein SEQ ID NO:357 is a clone designated herein as "UNQ211" and/or "DNA34353-1428".

Figure 145 shows the amino acid sequence (SEQ ID NO:358) derived from the coding sequence of SEQ ID NO:357 shown in Figure 144.

10 Figure 146 shows a nucleotide sequence (SEQ ID NO:362) of a native sequence PRO541 cDNA, wherein SEQ ID NO:362 is a clone designated herein as "UNQ342" and/or "DNA45417-1432".

Figure 147 shows the amino acid sequence (SEQ ID NO:363) derived from the coding sequence of SEQ ID NO:362 shown in Figure 146.

15 Figure 148 shows a nucleotide sequence (SEQ ID NO:369) of a native sequence PRO273 cDNA, wherein SEQ ID NO:369 is a clone designated herein as "UNQ240" and/or "DNA39523-1192".

Figure 149 shows the amino acid sequence (SEQ ID NO:370) derived from the coding sequence of SEQ ID NO:369 shown in Figure 148.

Figure 150 shows a nucleotide sequence (SEQ ID NO:374) of a native sequence PRO701 cDNA, wherein SEQ ID NO:374 is a clone designated herein as "UNQ365" and/or "DNA44205-1285".

20 Figure 151 shows the amino acid sequence (SEQ ID NO:375) derived from the coding sequence of SEQ ID NO:374 shown in Figure 150.

Figure 152 shows a nucleotide sequence (SEQ ID NO:379) of a native sequence PRO704 cDNA, wherein SEQ ID NO:379 is a clone designated herein as "UNQ368" and/or "DNA50911-1288".

25 Figure 153 shows the amino acid sequence (SEQ ID NO:380) derived from the coding sequence of SEQ ID NO:379 shown in Figure 152.

Figure 154 shows a nucleotide sequence (SEQ ID NO:384) of a native sequence PRO706 cDNA, wherein SEQ ID NO:384 is a clone designated herein as "UNQ370" and/or "DNA48329-1290".

Figure 155 shows the amino acid sequence (SEQ ID NO:385) derived from the coding sequence of SEQ ID NO:384 shown in Figure 154.

30 Figure 156 shows a nucleotide sequence (SEQ ID NO:389) of a native sequence PRO707 cDNA, wherein SEQ ID NO:389 is a clone designated herein as "UNQ371" and/or "DNA48306-1291".

Figure 157 shows the amino acid sequence (SEQ ID NO:390) derived from the coding sequence of SEQ ID NO:389 shown in Figure 156.

35 Figure 158 shows a nucleotide sequence (SEQ ID NO:394) of a native sequence PRO322 cDNA, wherein SEQ ID NO:394 is a clone designated herein as "UNQ283" and/or "DNA48336-1309".

Figure 159 shows the amino acid sequence (SEQ ID NO:395) derived from the coding sequence of SEQ

ID NO:394 shown in Figure 158.

Figure 160 shows a nucleotide sequence (SEQ ID NO:399) of a native sequence PRO526 cDNA, wherein SEQ ID NO:399 is a clone designated herein as "UNQ330" and/or "DNA44184-1319".

Figure 161 shows the amino acid sequence (SEQ ID NO:400) derived from the coding sequence of SEQ ID NO:399 shown in Figure 160.

5 Figure 162 shows a nucleotide sequence (SEQ ID NO:404) of a native sequence PRO531 cDNA, wherein SEQ ID NO:404 is a clone designated herein as "UNQ332" and/or "DNA48314-1320".

Figure 163 shows the amino acid sequence (SEQ ID NO:405) derived from the coding sequence of SEQ ID NO:404 shown in Figure 162.

10 Figure 164 shows a nucleotide sequence (SEQ ID NO:409) of a native sequence PRO534 cDNA, wherein SEQ ID NO:409 is a clone designated herein as "UNQ335" and/or "DNA48333-1321".

Figure 165 shows the amino acid sequence (SEQ ID NO:410) derived from the coding sequence of SEQ ID NO:409 shown in Figure 164.

Figure 166 shows a nucleotide sequence (SEQ ID NO:414) of a native sequence PRO697 cDNA, wherein SEQ ID NO:414 is a clone designated herein as "UNQ361" and/or "DNA50920-1325".

15 Figure 167 shows the amino acid sequence (SEQ ID NO:415) derived from the coding sequence of SEQ ID NO:414 shown in Figure 166.

Figure 168 shows a nucleotide sequence (SEQ ID NO:419) of a native sequence PRO717 cDNA, wherein SEQ ID NO:419 is a clone designated herein as "UNQ385" and/or "DNA50988-1326".

20 Figure 169 shows the amino acid sequence (SEQ ID NO:420) derived from the coding sequence of SEQ ID NO:419 shown in Figure 168.

Figures 170A-B show a nucleotide sequence (SEQ ID NO:424) of a native sequence PRO731 cDNA, wherein SEQ ID NO:424 is a clone designated herein as "UNQ395" and/or "DNA48321-1329".

Figure 171 shows the amino acid sequence (SEQ ID NO:425) derived from the coding sequence of SEQ ID NO:424 shown in Figures 170A-B.

25 Figure 172 shows a nucleotide sequence (SEQ ID NO:429) of a native sequence PRO218 cDNA, wherein SEQ ID NO:429 is a clone designated herein as "UNQ192" and/or "DNA30867-1335".

Figure 173 shows the amino acid sequence (SEQ ID NO:430) derived from the coding sequence of SEQ ID NO:429 shown in Figure 172.

Figure 174 shows an EST nucleotide sequence designated herein as DNA14472 (SEQ ID NO:431).

30 Figure 175 shows an EST nucleotide sequence designated herein as DNA15846 (SEQ ID NO:432).

Figures 176A-B show a nucleotide sequence (SEQ ID NO:436) of a native sequence PRO768 cDNA, wherein SEQ ID NO:436 is a clone designated herein as "UNQ406" and/or "DNA55737-1345".

Figure 177 shows the amino acid sequence (SEQ ID NO:437) derived from the coding sequence of SEQ ID NO:436 shown in Figures 176A-B.

35 Figure 178 shows a nucleotide sequence (SEQ ID NO:441) of a native sequence PRO771 cDNA, wherein SEQ ID NO:441 is a clone designated herein as "UNQ409" and/or "DNA49829-1346".

Figure 179 shows the amino acid sequence (SEQ ID NO:442) derived from the coding sequence of SEQ ID NO:441 shown in Figure 178.

Figures 180A-B show a nucleotide sequence (SEQ ID NO:446) of a native sequence PRO733 cDNA, wherein SEQ ID NO:446 is a clone designated herein as "UNQ411" and/or "DNA52196-1348".

Figure 181 shows the amino acid sequence (SEQ ID NO:447) derived from the coding sequence of SEQ ID NO:446 shown in Figures 180A-B.

Figure 182 shows a nucleotide sequence (SEQ ID NO:451) of a native sequence PRO162 cDNA, wherein SEQ ID NO:451 is a clone designated herein as "UNQ429" and/or "DNA46965-1356".

Figure 183 shows the amino acid sequence (SEQ ID NO:452) derived from the coding sequence of SEQ ID NO:451 shown in Figure 182.

Figure 184 shows a nucleotide sequence (SEQ ID NO:453) of a native sequence PRO788 cDNA, wherein SEQ ID NO:453 is a clone designated herein as "UNQ430" and/or "DNA56405-1357".

Figure 185 shows the amino acid sequence (SEQ ID NO:454) derived from the coding sequence of SEQ ID NO:453 shown in Figure 184.

Figure 186 shows a nucleotide sequence (SEQ ID NO:455) of a native sequence PRO1008 cDNA, wherein SEQ ID NO:455 is a clone designated herein as "UNQ492" and/or "DNA57530-1375".

Figure 187 shows the amino acid sequence (SEQ ID NO:456) derived from the coding sequence of SEQ ID NO:455 shown in Figure 186.

Figure 188 shows an EST nucleotide sequence designated herein as DNA16508 (SEQ ID NO:457).

Figures 189A-B show a nucleotide sequence (SEQ ID NO:458) of a native sequence PRO1012 cDNA, wherein SEQ ID NO:458 is a clone designated herein as "UNQ495" and/or "DNA56439-1376".

Figure 190 shows the amino acid sequence (SEQ ID NO:459) derived from the coding sequence of SEQ ID NO:458 shown in Figures 189A-B.

Figure 191 shows a nucleotide sequence (SEQ ID NO:463) of a native sequence PRO1014 cDNA, wherein SEQ ID NO:463 is a clone designated herein as "UNQ497" and/or "DNA56409-1377".

Figure 192 shows the amino acid sequence (SEQ ID NO:464) derived from the coding sequence of SEQ ID NO:463 shown in Figure 191.

Figure 193 shows a nucleotide sequence (SEQ ID NO:465) of a native sequence PRO1017 cDNA, wherein SEQ ID NO:465 is a clone designated herein as "UNQ500" and/or "DNA56112-1379".

Figure 194 shows the amino acid sequence (SEQ ID NO:466) derived from the coding sequence of SEQ ID NO:465 shown in Figure 193.

Figure 195 shows a nucleotide sequence (SEQ ID NO:467) of a native sequence PRO474 cDNA, wherein SEQ ID NO:467 is a clone designated herein as "UNQ502" and/or "DNA56045-1380".

Figure 196 shows the amino acid sequence (SEQ ID NO:468) derived from the coding sequence of SEQ ID NO:467 shown in Figure 195.

Figure 197 shows a nucleotide sequence (SEQ ID NO:469) of a native sequence PRO1031 cDNA, wherein SEQ ID NO:469 is a clone designated herein as "UNQ516" and/or "DNA59294-1381".

Figure 198 shows the amino acid sequence (SEQ ID NO:470) derived from the coding sequence of SEQ ID NO:469 shown in Figure 197.

Figure 199 shows a nucleotide sequence (SEQ ID NO:471) of a native sequence PRO938 cDNA, wherein SEQ ID NO:471 is a clone designated herein as "UNQ475" and/or "DNA56433-1406".

Figure 200 shows the amino acid sequence (SEQ ID NO:472) derived from the coding sequence of SEQ ID NO:471 shown in Figure 199.

Figure 201 shows a nucleotide sequence (SEQ ID NO:476) of a native sequence PRO1082 cDNA, wherein SEQ ID NO:476 is a clone designated herein as "UNQ539" and/or "DNA53912-1457".

Figure 202 shows the amino acid sequence (SEQ ID NO:477) derived from the coding sequence of SEQ ID NO:476 shown in Figure 201.

Figure 203 shows a nucleotide sequence (SEQ ID NO:482) of a native sequence PRO1083 cDNA, wherein SEQ ID NO:482 is a clone designated herein as "UNQ540" and/or "DNA50921-1458".

Figure 204 shows the amino acid sequence (SEQ ID NO:483) derived from the coding sequence of SEQ ID NO:482 shown in Figure 203.

Figure 205 shows an EST nucleotide sequence designated herein as DNA24256 (SEQ ID NO:484).

Figure 206 shows a nucleotide sequence (SEQ ID NO:487) of a native sequence PRO200 cDNA, wherein SEQ ID NO:487 is a clone designated herein as "UNQ174" and/or "DNA29101-1122".

Figure 207 shows the amino acid sequence (SEQ ID NO:488) derived from the coding sequence of SEQ ID NO:487 shown in Figure 206.

Figure 208 shows a nucleotide sequence (SEQ ID NO:495) of a native sequence PRO285 cDNA, wherein SEQ ID NO:495 is a clone designated herein as "DNA40021-1154".

Figure 209 shows the amino acid sequence (SEQ ID NO:496) derived from the coding sequence of SEQ ID NO:495 shown in Figure 208.

Figures 210A-B show a nucleotide sequence (SEQ ID NO:497) of a native sequence PRO286 cDNA, wherein SEQ ID NO:497 is a clone designated herein as "DNA42663-1154".

Figure 211 shows the amino acid sequence (SEQ ID NO:498) derived from the coding sequence of SEQ ID NO:497 shown in Figures 210A-B.

Figure 212 shows a nucleotide sequence (SEQ ID NO:505) of a native sequence PRO213-1 cDNA, wherein SEQ ID NO:505 is a clone designated herein as "DNA30943-1-1163-1".

Figure 213 shows the amino acid sequence (SEQ ID NO:506) derived from the coding sequence of SEQ ID NO:505 shown in Figure 212.

Figure 214 shows a nucleotide sequence (SEQ ID NO:507) of a native sequence PRO1330 cDNA, wherein SEQ ID NO:507 is a clone designated herein as "DNA64907-1163-1".

Figure 215 shows the amino acid sequence (SEQ ID NO:508) derived from the coding sequence of SEQ ID NO:507 shown in Figure 214.

Figure 216 shows a nucleotide sequence (SEQ ID NO:509) of a native sequence PRO1449 cDNA, wherein SEQ ID NO:509 is a clone designated herein as "DNA64908-1163-1".



Figure 217 shows the amino acid sequence (SEQ ID NO:510) derived from the coding sequence of SEQ ID NO:509 shown in Figure 216.

Figure 218 shows a nucleotide sequence (SEQ ID NO:514) of a native sequence PRO298 cDNA, wherein SEQ ID NO:514 is a clone designated herein as "UNQ261" and/or "DNA39975-1210".

Figure 219 shows the amino acid sequence (SEQ ID NO:515) derived from the coding sequence of SEQ ID NO:514 shown in Figure 218.

Figure 220 shows an EST nucleotide sequence designated herein as DNA26832 (SEQ ID NO:516).

Figure 221 shows a nucleotide sequence (SEQ ID NO:522) of a native sequence PRO337 cDNA, wherein SEQ ID NO:522 is a clone designated herein as "DNA43316-1237".

Figure 222 shows the amino acid sequence (SEQ ID NO:523) derived from the coding sequence of SEQ ID NO:522 shown in Figure 221.

Figure 223 shows an EST nucleotide sequence designated herein as DNA42301 (SEQ ID NO:524).

Figure 224 shows a nucleotide sequence (SEQ ID NO:525) of a native sequence PRO403 cDNA, wherein SEQ ID NO:525 is a clone designated herein as "DNA55800-1263".

Figure 225 shows the amino acid sequence (SEQ ID NO:526) derived from the coding sequence of SEQ ID NO:525 shown in Figure 224.

Figures 226A-B show an EST nucleotide sequence designated herein as DNA34415 (SEQ ID NO:527).

Figure 227 shows an EST nucleotide sequence designated herein as DNA49830 (SEQ ID NO:528).

Figure 228 shows an EST nucleotide sequence designated herein as DNA49831 (SEQ ID NO:529).

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## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

### I. Definitions

The terms "PRO polypeptide" and "PRO" as used herein and when immediately followed by a numerical designation refer to various polypeptides, wherein the complete designation (i.e., PRO/number) refers to specific polypeptide sequences as described herein. The terms "PRO/number polypeptide" and "PRO/number" as used herein encompass native sequence polypeptides and polypeptide variants (which are further defined herein). The PRO polypeptides described herein may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods.

A "native sequence PRO polypeptide" comprises a polypeptide having the same amino acid sequence as the corresponding PRO polypeptide derived from nature. Such native sequence PRO polypeptides can be isolated from nature or can be produced by recombinant or synthetic means. The term "native sequence PRO polypeptide" specifically encompasses naturally-occurring truncated or secreted forms of the specific PRO polypeptide (e.g., an extracellular domain sequence), naturally-occurring variant forms (e.g., alternatively spliced forms) and naturally-occurring allelic variants of the polypeptide. In various embodiments of the invention, the native sequence PRO213 polypeptide is a mature or full-length native sequence PRO213 polypeptide comprising amino acids 1 to 295 of Figure 2 (SEQ ID NO:2), the native sequence PRO274 polypeptide is a mature or full-length native sequence PRO274 polypeptide comprising amino acids 1 to 492

of Figure 4 (SEQ ID NO:7), the native sequence PRO300 polypeptide is a mature or full-length native sequence PRO300 polypeptide comprising amino acids 1 to 457 of Figure 9 (SEQ ID NO:19), the native sequence PRO284 polypeptide is a mature or full-length native sequence PRO284 polypeptide comprising amino acids 1 to 285 of Figure 11 (SEQ ID NO:28), the native sequence PRO296 polypeptide is a mature or full-length native sequence PRO296 polypeptide comprising amino acids 1 to 204 of Figure 15 (SEQ ID NO:36), the native sequence PRO329 polypeptide is a mature or full-length native sequence PRO329 polypeptide comprising amino acids 1 to 359 of Figure 20 (SEQ ID NO:45), the native sequence PRO362 polypeptide is a mature or full-length native sequence PRO362 polypeptide comprising amino acids 1 to 321 of Figure 22 (SEQ ID NO:52), the native sequence PRO363 polypeptide is a mature or full-length native sequence PRO363 polypeptide comprising amino acids 1 to 373 of Figure 24 (SEQ ID NO:59), the native sequence PRO868 polypeptide is a mature or full-length native sequence PRO868 polypeptide comprising amino acids 1 to 655 of Figure 26 (SEQ ID NO:64), the native sequence PRO382 polypeptide is a mature or full-length native sequence PRO382 polypeptide comprising amino acids 1 to 453 of Figure 28 (SEQ ID NO:69), the native sequence PRO545 polypeptide is a mature or full-length native sequence PRO545 polypeptide comprising amino acids 1 to 735 of Figure 30 (SEQ ID NO:74), the native sequence PRO617 polypeptide is a mature or full-length native sequence PRO617 polypeptide comprising amino acids 1 to 67 of Figure 33 (SEQ ID NO:85), the native sequence PRO700 polypeptide is a mature or full-length native sequence PRO700 polypeptide comprising amino acids 1 to 432 of Figure 35 (SEQ ID NO:90), the native sequence PRO702 polypeptide is a mature or full-length native sequence PRO702 polypeptide comprising amino acids 1 to 277 of Figure 37 (SEQ ID NO:97), the native sequence PRO703 polypeptide is a mature or full-length native sequence PRO703 polypeptide comprising amino acids 1 to 730 of Figure 39 (SEQ ID NO:102), the native sequence PRO705 polypeptide is a mature or full-length native sequence PRO705 polypeptide comprising amino acids 1 to 555 of Figure 41 (SEQ ID NO:109), the native sequence PRO708 polypeptide is a mature or full-length native sequence PRO708 polypeptide comprising amino acids 1 to 515 of Figure 43 (SEQ ID NO:114), the native sequence PRO320 polypeptide is a mature or full-length native sequence PRO320 polypeptide comprising amino acids 1 to 338 of Figure 45 (SEQ ID NO:119), the native sequence PRO324 polypeptide is a mature or full-length native sequence PRO324 polypeptide comprising amino acids 1 to 289 of Figure 47 (SEQ ID NO:124), the native sequence PRO351 polypeptide is a mature or full-length native sequence PRO351 polypeptide comprising amino acids 1 to 571 of Figure 49 (SEQ ID NO:132), the native sequence PRO352 polypeptide is a mature or full-length native sequence PRO352 polypeptide comprising amino acids 1 to 316 of Figure 51 (SEQ ID NO:137), the native sequence PRO381 polypeptide is a mature or full-length native sequence PRO381 polypeptide comprising amino acids 1 to 211 of Figure 53 (SEQ ID NO:145), the native sequence PRO386 polypeptide is a mature or full-length native sequence PRO386 polypeptide comprising amino acids 1 to 215 of Figure 55 (SEQ ID NO:150), the native sequence PRO540 polypeptide is a mature or full-length native sequence PRO540 polypeptide comprising amino acids 1 to 412 of Figure 59 (SEQ ID NO:157), the native sequence PRO615 polypeptide is a mature or full-length native sequence PRO615 polypeptide comprising amino acids 1 to 224 of Figure 61 (SEQ ID NO:162), the native sequence PRO618 polypeptide is a mature or full-length native sequence PRO618 polypeptide comprising amino acids 1 to 802 of

Figure 63 (SEQ ID NO:169), the native sequence PRO719 polypeptide is a mature or full-length native sequence PRO719 polypeptide comprising amino acids 1 to 354 of Figure 66 (SEQ ID NO:178), the native sequence PRO724 polypeptide is a mature or full-length native sequence PRO724 polypeptide comprising amino acids 1 to 713 of Figure 68 (SEQ ID NO:183), the native sequence PRO772 polypeptide is a mature or full-length native sequence PRO772 polypeptide comprising amino acids 1 to 152 of Figure 70 (SEQ ID NO:190), the native sequence PRO852 polypeptide is a mature or full-length native sequence PRO852 polypeptide comprising amino acids 1 to 518 of Figure 73 (SEQ ID NO:196), the native sequence PRO853 polypeptide is a mature or full-length native sequence PRO853 polypeptide comprising amino acids 1 to 377 of Figure 75 (SEQ ID NO:206), the native sequence PRO860 polypeptide is a mature or full-length native sequence PRO860 polypeptide comprising amino acids 1 to 985 of Figure 77 (SEQ ID NO:211), the native sequence PRO846 polypeptide is a mature or full-length native sequence PRO846 polypeptide comprising amino acids 1 to 332 of Figure 79 (SEQ ID NO:216), the native sequence PRO862 polypeptide is a mature or full-length native sequence PRO862 polypeptide comprising amino acids 1 to 146 of Figure 81 (SEQ ID NO:221), the native sequence PRO864 polypeptide is a mature or full-length native sequence PRO864 polypeptide comprising amino acids 1 to 351 of Figure 83 (SEQ ID NO:226), the native sequence PRO792 polypeptide is a mature or full-length native sequence PRO792 polypeptide comprising amino acids 1 to 293 of Figure 85 (SEQ ID NO:231), the native sequence PRO866 polypeptide is a mature or full-length native sequence PRO866 polypeptide comprising amino acids 1 to 331 of Figure 87 (SEQ ID NO:236), the native sequence PRO871 polypeptide is a mature or full-length native sequence PRO871 polypeptide comprising amino acids 1 to 472 of Figure 89 (SEQ ID NO:245), the native sequence PRO873 polypeptide is a mature or full-length native sequence PRO873 polypeptide comprising amino acids 1 to 545 of Figure 91 (SEQ ID NO:254), the native sequence PRO940 polypeptide is a mature or full-length native sequence PRO940 polypeptide comprising amino acids 1 to 544 of Figure 93 (SEQ ID NO:259), the native sequence PRO941 polypeptide is a mature or full-length native sequence PRO941 polypeptide comprising amino acids 1 to 772 of Figure 95 (SEQ ID NO:264), the native sequence PRO944 polypeptide is a mature or full-length native sequence PRO944 polypeptide comprising amino acids 1 to 211 of Figure 98 (SEQ ID NO:270), the native sequence PRO983 polypeptide is a mature or full-length native sequence PRO983 polypeptide comprising amino acids 1 to 243 of Figure 109 (SEQ ID NO:284), the native sequence PRO1057 polypeptide is a mature or full-length native sequence PRO1057 polypeptide comprising amino acids 1 to 413 of Figure 118 (SEQ ID NO:296), the native sequence PRO1071 polypeptide is a mature or full-length native sequence PRO1071 polypeptide comprising amino acids 1 to 525 of Figure 120 (SEQ ID NO:301), the native sequence PRO1072 polypeptide is a mature or full-length native sequence PRO1072 polypeptide comprising amino acids 1 to 336 of Figure 122 (SEQ ID NO:303), the native sequence PRO1075 polypeptide is a mature or full-length native sequence PRO1075 polypeptide comprising amino acids 1 to 406 of Figure 125 (SEQ ID NO:309), the native sequence PRO181 polypeptide is a mature or full-length native sequence PRO181 polypeptide comprising amino acids 1 to 144 of Figure 129 (SEQ ID NO:322), the native sequence PRO195 polypeptide is a mature or full-length native sequence PRO195 polypeptide comprising amino acids 1 to 323 of Figure 132 (SEQ ID NO:330), the native sequence PRO865 polypeptide is a mature or full-length native

sequence PRO865 polypeptide comprising amino acids 1 to 468 of Figure 136 (SEQ ID NO:337), the native sequence PRO827 polypeptide is a mature or full-length native sequence PRO827 polypeptide comprising amino acids 1 to 124 of Figure 39 (SEQ ID NO:346), the native sequence PRO1114 polypeptide is a mature or full-length native sequence PRO1114 polypeptide comprising amino acids 1 to 311 of Figure 142 (SEQ ID NO:352), the native sequence PRO237 polypeptide is a mature or full-length native sequence PRO237 polypeptide comprising amino acids 1 to 328 of Figure 145 (SEQ ID NO:358), the native sequence PRO541 polypeptide is a mature or full-length native sequence PRO541 polypeptide comprising amino acids 1 to 500 of Figure 147 (SEQ ID NO:363), the native sequence PRO273 polypeptide is a mature or full-length native sequence PRO273 polypeptide comprising amino acids 1 through 111 of Figure 149 (SEQ ID NO:370), the native sequence PRO701 polypeptide is a mature or full-length native sequence PRO701 polypeptide comprising amino acids 1 to 816 of Figure 151 (SEQ ID NO:375), the native sequence PRO704 polypeptide is a full-length or mature native sequence PRO704 polypeptide comprising amino acids 1 or 40 through 348 of Figure 153 (SEQ ID NO:380), the native sequence PRO706 polypeptide is a mature or full-length native sequence PRO706 polypeptide comprising amino acids 1 to 480 of Figure 155 (SEQ ID NO:385), the native sequence PRO707 polypeptide is a full-length or mature native sequence PRO707 polypeptide comprising amino acids 1 or 31 through 916 of Figure 157 (SEQ ID NO:390), the native sequence PRO322 polypeptide is a mature or full-length native sequence PRO322 polypeptide comprising amino acids 24 or 1 to 260 of Figure 159 (SEQ ID NO:395), the native sequence PRO526 polypeptide is a full-length or mature native sequence PRO526 polypeptide comprising amino acids 1 or 27 through 473 of Figure 161 (SEQ ID NO:400), the native sequence PRO531 polypeptide is a mature PRO531 polypeptide comprising amino acids 1 to 789 of Figure 163 (SEQ ID NO:405), the native sequence PRO534 polypeptide is a mature or full-length native sequence PRO534 polypeptide comprising amino acids 1 to 360 of Figure 165 (SEQ ID NO:410), the native sequence PRO697 polypeptide is a full-length or mature native sequence PRO697 polypeptide comprising amino acids 1 or 21 through 295 of Figure 167 (SEQ ID NO:415), the native sequence PRO717 polypeptide is a mature or full-length native sequence PRO717 polypeptide comprising amino acids 1 through 560 of Figure 169 (SEQ ID NO:420), the native sequence PRO731 polypeptide is a full-length or mature native sequence PRO731 polypeptide comprising amino acids 1 or 14 through 1184 of Figure 171 (SEQ ID NO:425), the native sequence PRO218 polypeptide is a full-length or mature native sequence PRO218 polypeptide comprising amino acids 1 or 24 through 455 of Figure 173 (SEQ ID NO:430), the native sequence PRO768 polypeptide is a full-length or mature native sequence PRO768 polypeptide comprising amino acids 1 or 34 through 1141 of Figure 177 (SEQ ID NO:437), the native sequence PRO771 polypeptide is a full-length or mature native sequence PRO771 polypeptide comprising amino acids 1 or 17 through 436 of Figure 179 (SEQ ID NO:442), the native sequence PRO733 polypeptide is a mature or full-length native sequence PRO733 polypeptide comprising amino acids 24 or 1 through 229 of Figure 181 (SEQ ID NO:447), the native sequence PRO162 polypeptide is a full-length or mature native sequence PRO162 polypeptide comprising amino acids 1 or 27 through 175 of Figure 183 (SEQ ID NO:452), the native sequence PRO788 polypeptide is a full-length or mature native sequence PRO788 polypeptide comprising amino acids 1 or 18 through 125 of Figure 185 (SEQ ID NO:454), the native sequence

PRO1008 polypeptide is a full-length or mature native sequence PRO1008 polypeptide comprising amino acids 1 or 24 through 266 of Figure 187 (SEQ ID NO:456), the native sequence PRO1012 polypeptide is a mature or full-length native sequence PRO1012 polypeptide comprising amino acids 1 through 747 of Figure 190 (SEQ ID NO:459), the native sequence PRO1014 polypeptide is a full-length or mature native sequence PRO1014 polypeptide comprising amino acids 1 or 20 through 300 of Figure 192 (SEQ ID NO:464), the native sequence

5 PRO1017 polypeptide is a full-length or mature native sequence PRO1017 polypeptide comprising amino acids 1 or 32 through 414 of Figure 194 (SEQ ID NO:466), the native sequence PRO474 polypeptide is a mature or full-length native sequence PRO474 polypeptide comprising amino acids 1 through 270 of Figure 196 (SEQ ID NO:468), the native sequence PRO1031 polypeptide is a full-length or mature native sequence PRO1031 polypeptide comprising amino acids 1 or 21 through 180 of Figure 198 (SEQ ID NO:470), the native sequence

10 PRO938 polypeptide is a mature or full-length native sequence PRO938 polypeptide comprising amino acids 1 to 349 of Figure 200 (SEQ ID NO:472), the native sequence PRO1082 polypeptide is a full-length or mature native sequence PRO1082 polypeptide comprising amino acids 1 through 201 of Figure 202 (SEQ ID NO:477), the native sequence PRO1083 polypeptide is a full-length or mature native sequence PRO1083 polypeptide comprising amino acids 1 or 26 through 693 of Figure 204 (SEQ ID NO:483), the native sequence VEGF-E

15 polypeptide is a mature or full-length native sequence VEGF-E polypeptide comprising amino acids 1 through 345 as depicted in Figure 207 (SEQ ID NO:488), the native sequence PRO285 is a mature or full-length native sequence PRO285 polypeptide comprising amino acids 1 to 1049 of Figure 209 (SEQ ID NO:496), the native sequence PRO286 is a mature or full-length native sequence PRO286 polypeptide comprising amino acids 1 to 1041 of Figure 211 (SEQ ID NO:298), the native sequence PRO298 is a mature or full-length native sequence

20 PRO298 comprising amino acids 1 to 364 of Figure 219 (SEQ ID NO:515), the native sequence PRO337 is a mature or full-length native sequence human neurotrophin comprising amino acids 1 to 344 of Figure 222 (SEQ ID NO:523), with or without the N-terminal signal sequence (residues 1 to about 28), and with or without the initiating methionine at position 1 and the native sequence PRO403 is a mature or full-length native sequence comprising amino acids 1 to 736 of Figure 225 (SEQ ID NO:526), with or without the initiating methionine at

25 position 1.

The PRO polypeptide "extracellular domain" or "ECD" refers to a form of the PRO polypeptide which is essentially free of the transmembrane and cytoplasmic domains. Ordinarily, a PRO polypeptide ECD will have less than 1% of such transmembrane and/or cytoplasmic domains and preferably, will have less than 0.5% of such domains. It will be understood that any transmembrane domains identified for the PRO polypeptides of

30 the present invention are identified pursuant to criteria routinely employed in the art for identifying that type of hydrophobic domain. The exact boundaries of a transmembrane domain may vary but most likely by no more than about 5 amino acids at either end of the domain as initially identified. Optionally, therefore, an extracellular domain of a PRO polypeptide may contain from about 5 or fewer amino acids on either or the transmembrane domain as initially identified.

35 "PRO polypeptide variant" means an active PRO polypeptide as defined above or below having at least about 80% amino acid sequence identity with the full-length native sequence PRO polypeptide sequence as

disclosed herein. Such PRO polypeptide variants include, for instance, PRO polypeptides wherein one or more amino acid residues are added, or deleted, at the N- or C-terminus of the full-length native amino acid sequence. Ordinarily, a PRO polypeptide variant will have at least about 80% amino acid sequence identity, more preferably at least about 85% amino acid sequence identity, and even more preferably at least about 90% amino acid sequence identity, even more preferably at least about 91% amino acid sequence identity, even more preferably at least about 92% amino acid sequence identity, even more preferably at least about 93% amino acid sequence identity, even more preferably at least about 94% amino acid sequence identity, even more preferably at least about 95% amino acid sequence identity, yet more preferably at least about 96% amino acid sequence identity, yet more preferably at least about 97% amino acid sequence identity, yet more preferably at least about 98% amino acid sequence identity and most preferably at least about 99% amino acid sequence identity with the amino acid sequence of the full-length native amino acid sequence as disclosed herein.

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. The preferred software alignment program is BLAST. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. The % identity values used herein have been generated using the WU-BLAST-2 computer program (Altschul et al., Methods in Enzymology 266:460-480 (1996); <http://blast.wustl.edu/blast/README.html>). Most of the WU-BLAST-2 search parameters were set to the default values. The adjustable parameters were set with the following values: overlap span = 1, overlap fraction = 0.125, word threshold (T) = 11, and scoring matrix = BLOSUM62. The HSP S and HSP S2 parameters, which are dynamic values used by BLAST-2, are established by the program itself depending upon the composition of the sequence of interest and composition of the database against which the sequence is being searched. However, the values may be adjusted to increase sensitivity. A % sequence identity value is determined by the fraction of matching identical residues divided by the total number of residues in the aligned region.

"Percent (%) nucleic acid sequence identity" with respect to PRO-encoding nucleic acid sequences identified herein is defined as the percentage of nucleotides in a candidate sequence that are identical with the nucleotides in the PRO nucleic acid sequence of interest, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity. Alignment for purposes of determining percent nucleic acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or Megalign (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any

algorithms needed to achieve maximal alignment over the full length of the sequences being compared. The identity values used herein were generated by the BLASTN module of WU-BLAST-2 set to the default parameters, with overlap span and overlap fraction set to 1 and 0.125, respectively.

The term "positives", in the context of sequence comparison performed as described above, includes residues in the sequences compared that are not identical but have similar properties (e.g. as a result of conservative substitutions). The % value of positives is determined by the fraction of residues scoring a positive value in the BLOSUM 62 matrix divided by the total number of residues in the aligned region, as defined above.

The term "epitope tagged" where used herein refers to a chimeric polypeptide comprising a PRO polypeptide, or domain sequence thereof, fused to a "tag polypeptide". The tag polypeptide has enough residues to provide an epitope against which an antibody may be made, or which can be identified by some other agent, yet is short enough such that it does not interfere with the activity of the PRO polypeptide of interest. The tag polypeptide preferably is also fairly unique so that the antibody does not substantially cross-react with other epitopes. Suitable tag polypeptides generally have at least six amino acid residues and usually between about 8 to about 50 amino acid residues (preferably, between about 10 to about 20 residues).

"Isolated," when used to describe the various polypeptides disclosed herein, means polypeptide that has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials that would typically interfere with diagnostic or therapeutic uses for the polypeptide, and may include enzymes, hormones, and other proteinaceous or non-proteinaceous solutes. In preferred embodiments, the polypeptide will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (2) to homogeneity by SDS-PAGE under non-reducing or reducing conditions using Coomassie blue or, preferably, silver stain. Isolated polypeptide includes polypeptide *in situ* within recombinant cells, since at least one component of the PRO polypeptide natural environment will not be present. Ordinarily, however, isolated polypeptide will be prepared by at least one purification step.

An "isolated" PRO polypeptide-encoding nucleic acid is a nucleic acid molecule that is identified and separated from at least one contaminant nucleic acid molecule with which it is ordinarily associated in the natural source of the PRO polypeptide nucleic acid. An isolated PRO polypeptide nucleic acid molecule is other than in the form or setting in which it is found in nature. Isolated PRO polypeptide nucleic acid molecules therefore are distinguished from the specific PRO polypeptide nucleic acid molecule as it exists in natural cells. However, an isolated PRO polypeptide nucleic acid molecule includes PRO polypeptide nucleic acid molecules contained in cells that ordinarily express the PRO polypeptide where, for example, the nucleic acid molecule is in a chromosomal location different from that of natural cells.

The term "control sequences" refers to DNA sequences necessary for the expression of an operably linked coding sequence in a particular host organism. The control sequences that are suitable for prokaryotes, for example, include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, polyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic

acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; or a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is accomplished by ligation at convenient restriction sites. If such sites do not exist, the synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice.

The term "antibody" is used in the broadest sense and specifically covers single anti-PRO polypeptide monoclonal antibodies (including agonist, antagonist, and neutralizing antibodies) and anti-PRO polypeptide antibody compositions with polyepitopic specificity. The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, *i.e.*, the individual antibodies comprising the population are identical except for possible naturally-occurring mutations that may be present in minor amounts.

"Active" or "activity" for the purposes herein refers to form(s) of PRO polypeptide which retain the biologic and/or immunologic activities of the specific native or naturally-occurring PRO polypeptide.

"Treatment" or "treating" refers to both therapeutic treatment and prophylactic or preventative measures. Those in need of treatment include those already with the disorder as well as those prone to have the disorder or those in which the disorder is to be prevented.

"Mammal" for purposes of treatment refers to any animal classified as a mammal, including humans, domestic and farm animals, and zoo, sports, or pet animals, such as sheep, dogs, horses, cats, cows, and the like. Preferably, the mammal herein is a human.

"Carriers" as used herein include pharmaceutically acceptable carriers, excipients, or stabilizers which are nontoxic to the cell or mammal being exposed thereto at the dosages and concentrations employed. Often the physiologically acceptable carrier is an aqueous pH buffered solution. Examples of physiologically acceptable carriers include buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptide; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEEN™, polyethylene glycol (PEG), and PLURONICS™.

The term "agonist" is used to refer to peptide and non-peptide analogs of the native PRO polypeptides (where native PRO polypeptide refers to pro-PRO polypeptide, pre-PRO polypeptide, prepro-PRO polypeptide, or mature PRO polypeptide) of the present invention and to antibodies specifically binding such native PRO polypeptides, provided that they retain at least one biological activity of a native PRO polypeptide. Preferably, the agonists of the present invention retain the qualitative binding recognition properties and receptor activation



properties of the native PRO polypeptide.

The term "antagonist" is used to refer to a molecule inhibiting a biological activity of a native PRO polypeptide of the present invention wherein native PRO polypeptide refers to pro-PRO polypeptide, pre-PRO polypeptide, prepro-PRO polypeptide, or mature PRO polypeptide. Preferably, the antagonists herein inhibit the binding of a native PRO polypeptide of the present invention to a binding partner. A PRO polypeptide

- 5 "antagonist" is a molecule which prevents, or interferes with, a PRO antagonist effector function (*e.g.* a molecule which prevents or interferes with binding and/or activation of a PRO polypeptide receptor by PRO polypeptide). Such molecules can be screened for their ability to competitively inhibit PRO polypeptide receptor activation by monitoring binding of native PRO polypeptide in the presence and absence of the test antagonist molecule, for example. An antagonist of the invention also encompasses an antisense polynucleotide against the PRO
- 10 polypeptide gene, which antisense polynucleotide blocks transcription or translation of the PRO polypeptide gene, thereby inhibiting its expression and biological activity.

"Stringency" of hybridization reactions is readily determinable by one of ordinary skill in the art, and generally is an empirical calculation dependent upon probe length, washing temperature, and salt concentration. In general, longer probes require higher temperatures for proper annealing, while shorter probes need lower

15 temperatures. Hybridization generally depends on the ability of denatured DNA to reanneal when complementary strands are present in an environment below their melting temperature. The higher the degree of desired homology between the probe and hybridizable sequence, the higher the relative temperature which can be used. As a result, it follows that higher relative temperatures would tend to make the reaction conditions more stringent, while lower temperatures less so. For additional details and explanation of stringency of

20 hybridization reactions, see Ausubel *et al.*, Current Protocols in Molecular Biology, Wiley Interscience Publishers, (1995).

- "Stringent conditions" means (1) employing low ionic strength and high temperature for washing, for example, 0.015 sodium chloride/0.0015 M sodium citrate/0.1% sodium dodecyl sulfate at 50°C, or (2) employing during hybridization a denaturing agent, such as formamide, for example, 50% (vol/vol) formamide
- 25 with 0.1% bovine serum albumin/0.1% Ficoll/0.1% polyvinylpyrrolidone/50 mM sodium phosphate buffer at pH 6.5 with 750 mM sodium chloride, 75 mM sodium citrate at 42°C. Another example is use of 50% formamide, 5 x SSC (0.75 M NaCl, 0.075 M sodium citrate), 50 mM sodium phosphate (pH 6/8), 0.1% sodium pyrophosphate, 5 x Denhardt's solution, sonicated salmon sperm DNA (50 µg/ml), 0.1% SDS, and 10% dextran sulfate at 42°C, with washes at 42°C in 0.2 x SSC and 0.1% SDS. Yet another example is hybridization using
- 30 a buffer of 10% dextran sulfate, 2 x SSC (sodium chloride/sodium citrate) and 50% formamide at 55°C, followed by a high-stringency wash consisting of 0.1 x SSC containing EDTA at 55°C.

- "Moderately stringent conditions" are described in Sambrook *et al.*, *supra*, and include the use of a washing solution and hybridization conditions (*e.g.*, temperature, ionic strength, and %SDS) less stringent than described above. An example of moderately stringent conditions is a condition such as overnight incubation at
- 35 37°C in a solution comprising: 20% formamide, 5 x SSC (150 mM NaCl, 15 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5 x Denhardt's solution, 10% dextran sulfate, and 20 mg/mL denatured sheared

salmon sperm DNA, followed by washing the filters in 1 x SSC at about 37-50°C. The skilled artisan will recognize how to adjust the temperature, ionic strength, *etc.*, as necessary to accommodate factors such as probe length and the like.

"Southern analysis" or "Southern blotting" is a method by which the presence of DNA sequences in a restriction endonuclease digest of DNA or a DNA-containing composition is confirmed by hybridization to a known, labeled oligonucleotide or DNA fragment. Southern analysis typically involves electrophoretic separation of DNA digests on agarose gels, denaturation of the DNA after electrophoretic separation, and transfer of the DNA to nitrocellulose, nylon, or another suitable membrane support for analysis with a radiolabeled, biotinylated, or enzyme-labeled probe as described in sections 9.37-9.52 of Sambrook *et al.*, Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press, 1989).

"Northern analysis" or "Northern blotting" is a method used to identify RNA sequences that hybridize to a known probe such as an oligonucleotide, DNA fragment, cDNA or fragment thereof, or RNA fragment. The probe is labeled with a radioisotope such as <sup>32</sup>P, or by biotinylation, or with an enzyme. The RNA to be analyzed is usually electrophoretically separated on an agarose or polyacrylamide gel, transferred to nitrocellulose, nylon, or other suitable membrane, and hybridized with the probe, using standard techniques well known in the art such as those described in sections 7.39-7.52 of Sambrook *et al.*, *supra*.

As used herein, the term "immunoadhesin" designates antibody-like molecules which combine the binding specificity of a heterologous protein (an "adhesin") with the effector functions of immunoglobulin constant domains. Structurally, the immunoadhesins comprise a fusion of an amino acid sequence with the desired binding specificity which is other than the antigen recognition and binding site of an antibody (i.e., is "heterologous"), and an immunoglobulin constant domain sequence. The adhesin part of an immunoadhesin molecule typically is a contiguous amino acid sequence comprising at least the binding site of a receptor or a ligand. The immunoglobulin constant domain sequence in the immunoadhesin may be obtained from any immunoglobulin, such as IgG-1, IgG-2, IgG-3, or IgG-4 subtypes, IgA (including IgA-1 and IgA-2), IgE, IgD or IgM.

"Chronic" administration refers to administration of the agent(s) in a continuous mode as opposed to an acute mode, so as to maintain the initial therapeutic effect (activity) for an extended period of time. "Intermittent" administration is treatment that is not consecutively done without interruption, but rather is cyclic in nature.

Administration "in combination with" one or more further therapeutic agents includes simultaneous (concurrent) and consecutive administration in any order.

As used herein, "vascular endothelial cell growth factor-E," or "VEGF-E," refers to a mammalian growth factor as described herein, including the human amino acid sequence of Figure 207, a sequence which has homology to VEGF and bone morphogenetic protein 1 and which includes complete conservation of all VEGF cysteine residues, which have been shown to be required for biological activity of VEGF. VEGF-E expression includes expression in human fetal bone, thymus, and the gastrointestinal tract. The biological activity of native VEGF-E is shared by any analogue or variant thereof that is capable of promoting selective

growth and/or survival of umbilical vein endothelial cells, induces proliferation of pluripotent fibroblast cells, induces immediate early gene c-fos in human endothelial cell lines and causes myocyte hypertrophy in cardiac cells, or which possesses an immune epitope that is immunologically cross-reactive with an antibody raised against at least one epitope of the corresponding native VEGF-E. The human VEGF-E herein is active on rat and mouse cells indicating conservation across species. Moreover, the VEGF-E herein is expressed at the growth plate region and has been shown to embrace fetal myocytes.

As used herein, "vascular endothelial cell growth factor," or "VEGF," refers to a mammalian growth factor as defined in U.S. Patent 5,332,671. The biological activity of native VEGF is shared by any analogue or variant thereof that is capable of promoting selective growth of vascular endothelial cells but not of bovine corneal endothelial cells, lens epithelial cells, adrenal cortex cells, BHK-21 fibroblasts, or keratinocytes, or that possesses an immune epitope that is immunologically cross-reactive with an antibody raised against at least one epitope of the corresponding native VEGF.

The terms "VEGF-E polypeptide" and "VEGF-E" when used herein encompass native sequence VEGF-E polypeptide and VEGF-E polypeptide variants (which are further defined herein). The VEGF-E polypeptides may be isolated from a variety of sources, such as from human tissue types or from another source, or prepared by recombinant or synthetic methods.

Inhibitors of VEGF-E include those which reduce or inhibit the activity or expression of VEGF-E and includes antisense molecules.

The abbreviation "KDR" refers to the kinase domain region of the VEGF molecule. VEGF-E has no homology with VEGF in this domain.

The abbreviation "FLT-1" refers to the FMS-like tyrosine kinase binding domain which is known to bind to the corresponding FLT-1 receptor. VEGF-E has no homology with VEGF in this domain.

"Toll receptor 2", "TLR2" and "huTLR2" are used interchangeably, and refer to a human Toll receptor designated as "HuTLR2" by Rock *et al.*, *Proc. Natl. Acad. Sci. USA* 95, 588-593 (1998).

The term "expression vector" is used to define a vector, in which a nucleic acid encoding a PRO polypeptide herein is operably linked to control sequences capable of affecting its expression is a suitable host cells. Vectors ordinarily carry a replication site (although this is not necessary where chromosomal integration will occur). Expression vectors also include marker sequences which are capable of providing phenotypic selection in transformed cells. For example, *E. coli* is typically transformed using pBR322, a plasmid derived from an *E. coli* species (Bolivar, *et al.*, *Gene* 2: 95 [1977]). pBR322 contains genes for ampicillin and tetracycline resistance and thus provides easy means for identifying transformed cells, whether for purposes of cloning or expression. Expression vectors also optimally will contain sequences which are useful for the control of transcription and translation, e.g., promoters and Shine-Dalgarno sequences (for prokaryotes) or promoters and enhancers (for mammalian cells). The promoters may be, but need not be, inducible; even powerful constitutive promoters such as the CMV promoter for mammalian hosts have been found to produce the LHR without host cell toxicity. While it is conceivable that expression vectors need not contain any expression control, replicative sequences or selection genes, their absence may hamper the identification of hybrid

transformants and the achievement of high level hybrid immunoglobulin expression.

The term "lipopolysaccharide" or "LPS" is used herein as a synonym of "endotoxin." Lipopolysaccharides (LPS) are characteristic components of the outer membrane of Gram-negative bacteria, e.g., *Escherichia coli*. They consist of a polysaccharide part and a fat called lipid A. The polysaccharide, which varies from one bacterial species to another, is made up of the O-specific chain (built from repeating units of three to eight sugars) and the two-part core. Lipid A virtually always includes two glucosamine sugars modified by phosphate and a variable number of fatty acids. For further information see, for example, Rietschel and Brade, Scientific American August 1992, 54-61.

The term "septic shock" is used herein in the broadest sense, including all definitions disclosed in Bone, Ann. Intern. Med. 114, 332-333 (1991). Specifically, septic shock starts with a systemic response to infection, a syndrome called sepsis. When this syndrome results in hypotension and organ dysfunction, it is called septic shock. Septic shock may be initiated by gram-positive organisms and fungi, as well as endotoxin-containing Gram-negative organisms. Accordingly, the present definition is not limited to "endotoxin shock."

The phrases "gene amplification" and "gene duplication" are used interchangeably and refer to a process by which multiple copies of a gene or gene fragment are formed in a particular cell or cell line. The duplicated region (a stretch of amplified DNA) is often referred to as "amplicon". Usually, the amount of the messenger RNA (mRNA) produced, i.e., the level of gene expression, also increases in the proportion of the number of copies made of the particular gene expressed.

"Tumor", as used herein, refers to all neoplastic cell growth and proliferation, whether malignant or benign, and all pre-cancerous and cancerous cells and tissues. The terms "cancer" and "cancerous" refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth. Examples of cancer include but are not limited to, carcinoma, lymphoma, blastoma, sarcoma, and leukemia. More particular examples of such cancers include breast cancer, prostate cancer, colon cancer, pancreatic cancer, small-cell lung cancer, non-small cell lung cancer, gastrointestinal cancer, pancreatic cancer, glioblastoma, cervical cancer, ovarian cancer, liver cancer, bladder cancer, hepatoma, colorectal cancer, endometrial carcinoma, salivary gland carcinoma, kidney cancer, vulval cancer, thyroid cancer, hepatic carcinoma and various types of head and neck cancer.

The term "cytotoxic agent" as used herein refers to a substance that inhibits or prevents the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes (e.g. I131, I125, Y90 and Re186), chemotherapeutic agents, and toxins such as enzymatically active toxins of bacterial, fungal, plant or animal origin, or fragments thereof.

A "chemotherapeutic agent" is a chemical compound useful in the treatment of cancer. Examples of chemotherapeutic agents include adriamycin, doxorubicin, epirubicin, 5-fluorouracil, cytosine arabinoside ("Ara-C"), cyclophosphamide, thiotepa, busulfan, cytoxin, taxoids, e.g. paclitaxel (Taxol, Bristol-Myers Squibb Oncology, Princeton, NJ), and doxetaxel (Taxotere, Rhone-Poulenc Rorer, Antony, France), toxtotere, methotrexate, cisplatin, melphalan, vinblastine, bleomycin, etoposide, ifosfamide, mitomycin C, mitoxantrone, vincristine, vinorelbine, carboplatin, teniposide, daunomycin, carminomycin, aminopterin, dactinomycin,

mitomycins, esperamicins (see U.S. Pat. No. 4,675,187); melphalan and other related nitrogen mustards. Also included in this definition are hormonal agents that act to regulate or inhibit hormone action on tumors such as tamoxifen and onapristone.

A "growth inhibitory agent" when used herein refers to a compound or composition which inhibits growth of a cell, especially cancer cell overexpressing any of the genes identified herein, either in vitro or in vivo. Thus, the growth inhibitory agent is one which significantly reduces the percentage of cells overexpressing such genes in S phase. Examples of growth inhibitory agents include agents that block cell cycle progression (at a place other than S phase), such as agents that induce G1 arrest and M-phase arrest. Classical M-phase blockers include the vincas (vincristine and vinblastine), taxol, and topo II inhibitors such as doxorubicin, epirubicin, daunorubicin, etoposide, and bleomycin. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C. Further information can be found in The Molecular Basis of Cancer, Mendelsohn and Israel, eds., Chapter 1, entitled "Cell cycle regulation, oncogens, and antineoplastic drugs" by Murakami et al. (WB Saunders: Philadelphia, 1995), especially p.13.

"Doxorubicin" is an anthracycline antibiotic.

The term "cytokine" is a generic term for proteins released by one cell population which act on another cell as intercellular mediators. Examples of such cytokines are lymphokines, monokines, and traditional polypeptide hormones. Included among the cytokines are growth hormone such as human growth hormone, N-methionyl human growth hormone, and bovine growth hormone; parathyroid hormone; thyroxine; insulin; proinsulin; relaxin; prolaxin; and the like. As used herein, the term cytokine includes proteins from natural sources or from recombinant cell culture and biologically active equivalents of the native sequence cytokines.

"Immunological cross-reactivity" as used herein means that the candidate polypeptide is capable of competitively inhibiting the qualitative biological activity of a PRO213-1, PRO1330, or PRO1449 polypeptide having this activity with polyclonal antisera raised against the known active PRO213-1, PRO1330, or PRO1449 polypeptide. Such antisera may be prepared in conventional fashion by injecting goats or rabbits, for example, subcutaneously with the known active analogue in complete Freund's adjuvant, followed by booster intraperitoneal or subcutaneous injection in incomplete Freund's. The immunological cross-reactivity preferably is "specific", which means that the binding affinity of the immunological cross-reactive molecule (e.g., antibody) identified, to the corresponding PRO213-1, PRO1330, or PRO1449 polypeptide is significantly higher (preferably at least about 2-times, more preferably at least about 4-times, even more preferably at least about 6-times, most preferably at least about 8-times higher) than the binding affinity of that molecule to any other known native polypeptide.

"Native antibodies" and "native immunoglobulins" are usually heterotetrameric glycoproteins of about 150,000 daltons, composed of two identical light (L) chains and two identical heavy (H) chains. Each light chain is linked to a heavy chain by one covalent disulfide bond, while the number of disulfide linkages varies among the heavy chains of different immunoglobulin isotypes. Each heavy and light chain also has regularly spaced intrachain disulfide bridges. Each heavy chain has at one end a variable domain (VH) followed by a

number of constant domains. Each light chain has a variable domain at one end (VL) and a constant domain at its other end; the constant domain of the light chain is aligned with the first constant domain of the heavy chain, and the light chain variable domain is aligned with the variable domain of the heavy chain. Particular amino acid residues are believed to form an interface between the light- and heavy-chain variable domains.

The term "variable" refers to the fact that certain portions of the variable domains differ extensively in sequence among antibodies and are used in the binding and specificity of each particular antibody for its particular antigen. However, the variability is not evenly distributed throughout the variable domains of antibodies. It is concentrated in three segments called complementarity-determining regions (CDRs) or hypervariable regions both in the light-chain and the heavy-chain variable domains. The more highly conserved portions of variable domains are called the framework (FR). The variable domains of native heavy and light chains each comprise four FR regions, largely adopting a  $\beta$ -sheet configuration, connected by three CDRs, which form loops connecting, and in some cases forming part of, the  $\beta$ -sheet structure. The CDRs in each chain are held together in close proximity by the FR regions and, with the CDRs from the other chain, contribute to the formation of the antigen-binding site of antibodies (see Kabat et al., NIH Publ. No.91-3242, Vol. I, pages 647-669 (1991)). The constant domains are not involved directly in binding an antibody to an antigen, but exhibit various effector functions, such as participation of the antibody in antibody-dependent cellular toxicity.

"Antibody fragments" comprise a portion of an intact antibody, preferably the antigen binding or variable region of the intact antibody. Examples of antibody fragments include Fab, Fab', F(ab')<sub>2</sub>, and Fv fragments; diabodies; linear antibodies (Zapata et al., Protein Eng. 8(10): 1057-1062 [1995]); single-chain antibody molecules; and multispecific antibodies formed from antibody fragments.

Papain digestion of antibodies produces two identical antigen-binding fragments, called "Fab" fragments, each with a single antigen-binding site, and a residual "Fc" fragment, a designation reflecting the ability to crystallize readily. Pepsin treatment yields an F(ab')<sub>2</sub> fragment that has two antigen-combining sites and is still capable of cross-linking antigen.

"Fv" is the minimum antibody fragment which contains a complete antigen-recognition and -binding site. This region consists of a dimer of one heavy- and one light-chain variable domain in tight, non-covalent association. It is in this configuration that the three CDRs of each variable domain interact to define an antigen-binding site on the surface of the VH-VL dimer. Collectively, the six CDRs confer antigen-binding specificity to the antibody. However, even a single variable domain (or half of an Fv comprising only three CDRs specific for an antigen) has the ability to recognize and bind antigen, although at a lower affinity than the entire binding site.

The Fab fragment also contains the constant domain of the light chain and the first constant domain (CH1) of the heavy chain. Fab fragments differ from Fab fragments by the addition of a few residues at the carboxy terminus of the heavy chain CH1 domain including one or more cysteines from the antibody hinge region. Fab'-SH is the designation herein for Fab' in which the cysteine residue(s) of the constant domains bear a free thiol group. F(ab')<sub>2</sub> antibody fragments originally were produced as pairs of Fab' fragments which have hinge cysteines between them. Other chemical couplings of antibody fragments are also known.

The "light chains" of antibodies (immunoglobulins) from any vertebrate species can be assigned to one of two clearly distinct types, called kappa and lambda, based on the amino acid sequences of their constant domains.

Depending on the amino acid sequence of the constant domain of their heavy chains, immunoglobulins can be assigned to different classes. There are five major classes of immunoglobulins: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA<sub>1</sub>, and IgA<sub>2</sub>.

"Single-chain Fv" or "sFv" antibody fragments comprise the VH and VL domains of antibody, wherein these domains are present in a single polypeptide chain. Preferably, the Fv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the sFv to form the desired structure for antigen binding. For a review of sFv see Pluckthun in The Pharmacology of Monoclonal Antibodies, vol. 113, Rosenberg and Moore eds., Springer-Verlag, New York, pp. 269-315 (1994).

The term "diabodies" refers to small antibody fragments with two antigen-binding sites, which fragments comprise a heavy-chain variable domain (VH) connected to a light-chain variable domain (VL) in the same polypeptide chain (VH - VL). By using a linker that is too short to allow pairing between the two domains on the same chain, the domains are forced to pair with the complementary domains of another chain and create two antigen-binding sites. Diabodies are described more fully in, for example, EP 404,097; WO 93/11161; and Hollinger et al., Proc. Natl. Acad. Sci. USA, 90:6444-6448 (1993).

An "isolated" antibody is one which has been identified and separated and/or recovered from a component of its natural environment. Contaminant components of its natural environment are materials which would interfere with diagnostic or therapeutic uses for the antibody, and may include enzymes, hormones, and other proteinaceous or nonproteinaceous solutes. In preferred embodiments, the antibody will be purified (1) to a degree sufficient to obtain at least 15 residues of N-terminal or internal amino acid sequence by use of a spinning cup sequenator, or (3) to homogeneity by SDS-PAGE under reducing or nonreducing conditions using Coomassie blue or, preferably, silver stain. Isolated antibody includes the antibody in situ within recombinant cells since at least one component of the antibody's natural environment will not be present. Ordinarily, however, isolated antibody will be prepared by at least one purification step.

The word "label" when used herein refers to a detectable compound or composition which is conjugated directly or indirectly to the antibody so as to generate a "labelled" antibody. The label may be detectable by itself (e.g. radioisotope labels or fluorescent labels) or, in the case of an enzymatic label, may catalyze chemical alteration of a substrate compound or composition which is detectable.

By "solid phase" is meant a non-aqueous matrix to which the antibody of the present invention can adhere. Examples of solid phases encompassed herein include those formed partially or entirely of glass (e.g., controlled pore glass), polysaccharides (e.g., agarose), polyacrylamides, polystyrene, polyvinyl alcohol and silicones. In certain embodiments, depending on the context, the solid phase can comprise the well of an assay plate; in others it is a purification column (e.g., an affinity chromatography column). This term also includes

a discontinuous solid phase of discrete particles, such as those described in U.S. Patent No. 4,275,149.

A "liposome" is a small vesicle composed of various types of lipids, phospholipids and/or surfactant which is useful for delivery of a drug (such as the anti-ErbB2 antibodies disclosed herein and, optionally, a chemotherapeutic agent) to a mammal. The components of the liposome are commonly arranged in a bilayer formation, similar to the lipid arrangement of biological membranes.

5

## II. Compositions and Methods of the Invention

### 1. Full-length PRO213 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO213. In particular, Applicants have identified and isolated cDNA  
10 encoding a PRO213 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that a portion of the PRO213 polypeptide has significant homology with the human growth arrest-specific 6 (gas6) protein. Accordingly, it is presently believed that PRO213 polypeptide disclosed in the present application may have the same or similar activity as does the  
15 gas6 protein.

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### 2. Full-length PRO274 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO274. In particular, Applicants have identified and isolated cDNA  
20 encoding a PRO274 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO274 polypeptide have significant homology with the 7 transmembrane segment receptor proteins and Fn54 protein. Accordingly, it is presently believed that PRO274 polypeptide disclosed in the present application is a newly identified member  
of the 7 transmembrane segment receptor protein and/or Fn54 protein family.

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### 3. Full-length PRO300 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO300. In particular, Applicants have identified and isolated cDNA  
30 encoding a PRO300 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO300 polypeptide have significant homology with the human Diff 33 protein. Accordingly, it is presently believed that PRO300 polypeptide disclosed in the present application is a newly identified member of the Diff 33 family.

### 4. Full-length PRO284 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides  
35 referred to in the present application as PRO284. In particular, Applicants have identified and isolated cDNA encoding a PRO284 polypeptide, as disclosed in further detail in the Examples below. To Applicants present



knowledge, the UNQ247 (DNA23318-1211) nucleotide sequence encodes a novel factor; using BLAST and FastA sequence alignment computer programs, no sequence identities to any known proteins were revealed.

5. **Full-length PRO296 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO296. In particular, Applicants have identified and isolated cDNA encoding a PRO296 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO296 polypeptide has significant similarity to the sarcoma-amplified SAS protein. Accordingly, it is presently believed that PRO296 polypeptide disclosed in the present application is a newly identified SAS protein homolog.

6. **Full-length PRO329 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO329. In particular, Applicants have identified and isolated cDNA encoding a PRO329 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO329 polypeptide has significant similarity to a high affinity immunoglobulin F<sub>c</sub> receptor. Accordingly, it is presently believed that PRO329 polypeptide disclosed in the present application is a newly identified F<sub>c</sub> receptor homolog.

7. **Full-length PRO362 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO362. In particular, Applicants have identified and isolated cDNA encoding a PRO362 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO362 polypeptide has significant similarity to the A33 antigen protein as well as the HCAR protein and the NrCAM related cell adhesion molecule. Accordingly, it is presently believed that PRO362 polypeptide disclosed in the present application is a newly A33 antigen and HCAR protein homolog.

8. **Full-length PRO363 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO363. In particular, Applicants have identified and isolated cDNA encoding a PRO363 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO363 polypeptide has significant similarity to the cell surface protein HCAR. Accordingly, it is presently believed that PRO363 polypeptide disclosed in the present application is a newly HCAR homolog.

9. Full-length PRO868 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO868. In particular, Applicants have identified and isolated cDNA encoding a PRO868 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO868 polypeptide has significant similarity to the tumor necrosis factor receptor. Accordingly, it is presently believed that PRO868 polypeptide disclosed in the present application is a newly identified member of the tumor necrosis factor receptor family of proteins.

10. Full-length PRO382 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO382. In particular, Applicants have identified and isolated cDNA encoding a PRO382 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the native PRO382 polypeptide shares significant homology with various serine protease proteins. Applicants have also found that the DNA encoding the PRO382 polypeptide shares significant homology with nucleic acid encoding various serine protease proteins. Accordingly, it is presently believed that PRO382 polypeptide disclosed in the present application is a newly identified serine protease homolog.

11. Full-length PRO545 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO545. In particular, Applicants have identified and isolated cDNA encoding a PRO545 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO545 polypeptide have significant homology with the sequences identified designated as; human metalloproteinase ("P\_W01825"), mouse meltrinalpha ("S60257"), metalloprotease-disintegrin meltrin-alpha ("GEN13695"), ADAM 13 - *Xenopus laevis* ("XLU66003\_1"), mouse meltrin beta ("S60258"), rabbit metalloprotease-disintegrin meltrin-beta, ("GEN13696"), human meltrin S ("AF023477\_1"), human meltrin precursor ("AF023476\_1"), human ADAM 21 ("AF029900\_1"), and human ADAM 20 ("AF029899\_1"), thereby indicating that PRO545 may be a novel meltrin protein. Accordingly, it is presently believed that the PRO545 polypeptide disclosed in the present application is a newly identified member of the meltrin family and possesses the cellular adhesiveness typical of the meltrin proteins which comprise both metalloprotease and disintegrin domains.

12. Full-length PRO617 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO617. In particular, Applicants have identified and isolated cDNA encoding a PRO617 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO617 polypeptide shares significant

homology with the CD24 protein. Applicants have also found that the DNA encoding the PRO617 polypeptide has significant homology with DNA encoding the CD24 protein. Accordingly, it is presently believed that PRO617 polypeptide disclosed in the present application is a newly identified CD24 homolog.

### 13. Full-length PRO700 Polypeptides

5 The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO700. In particular, Applicants have identified and isolated cDNA encoding a PRO700 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO700 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO700 polypeptide possess significant sequence similarity to  
 10 various protein disulfide isomerases. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO700 amino acid sequence and the following Dayhoff sequences; polypeptide with protein disulfide isomerase activity, designated as ("P\_P80664"), human PDI, designated as ("P\_R51696"), human PDI, designated as (P\_R25297"), probable protein disulfide isomerase er-60 precursor, designated as ("ER60\_SCHMA"), protein disulfide isomerase precursor - *Drosophila*  
 15 *melanogaster*, designated as ("PDI\_DROME"), protein disulfide-isomerase precursor - *Nicotiana tabaccum*, designated as ("NTPDIGENE\_1"), protein disulfide isomerase - *Onchocerca volvulus*, designated as ("OVU12440\_1"), human probable protein disulfide isomerase p5 precursor, designated as ("ERP5\_HUMAN"), human protein disulfide isomerase-related protein 5, ("HSU79278\_1"), and protein disulfide isomerase precursor / prolyl 4- hydroxy, ("PDI\_HUMAN"), thereby indicating that PRO700 may be  
 20 a novel protein disulfide isomerase. Accordingly, it is presently believed that PRO700 polypeptide disclosed in the present application is a newly identified member of the protein disulfide isomerase family and possesses the ability to catalyze the formation of disulfide bonds typical of the protein disulfide isomerase family.

### 14. Full-length PRO702 Polypeptides

25 The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO702. In particular, Applicants have identified and isolated cDNA encoding a PRO702 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO702 polypeptide has significant similarity to the conglutinin protein. Accordingly, it is presently believed that PRO702 polypeptide disclosed in the present  
 30 application is a newly identified conglutinin homolog.

### 15. Full-length PRO703 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO703. In particular, Applicants have identified and isolated cDNA  
 35 encoding a PRO703 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO703 polypeptide using BLAST and FastA sequence alignment computer

programs, suggests that various portions of the PRO703 polypeptide possess significant sequence similarity to the VLCAS protein, thereby indicating that PRO703 may be a novel VLCAS protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO703 amino acid sequence and the following Dayhoff sequences, human mRNA for very-long-chain acyl-CoA, ("D88308"), rat mRNA for very-long-chain acyl-CoA synthetase, ("D85100"), *Mus musculus* fatty acid transport protein, ("MMU15976"), human very-long-chain acyl-CoA synthetase, ("D88308\_1"), *Mus musculus* very-long-chain acyl-CoA synthetase, ("AF033031\_1"), very-long-chain acyl-CoA synthetase - *Rattus*, ("D85100\_1"), rat long-chain fatty acid transport protein, ("FATP\_RAT"), mouse long-chain fatty acid transport protein, ("FATP\_MOUSE"), probable long-chain fatty acid transport protein, ("FAT1\_YEAST"), and fatty acid transporter protein, ("CHY15839\_2"), thereby indicating that PRO703 may be a novel VLCAS. Accordingly, it is presently believed that PRO703 polypeptide disclosed in the present application is a newly identified member of the VLCAS family and possesses the ability to facilitate the cellular transport of long and very long chain fatty acids typical of the VLCAS family.

#### 16. Full-length PRO705 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO705. In particular, Applicants have identified and isolated cDNA encoding a PRO705 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO705 polypeptide has significant similarity to the K-glypican protein. Accordingly, it is presently believed that PRO705 polypeptide disclosed in the present application is a newly identified member of the glypican family of proteoglycan proteins.

#### 17. Full-length PRO708 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO708. In particular, Applicants have identified and isolated cDNA encoding a PRO708 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO708 polypeptide has significant homology with the aryl sulfatase proteins. Applicants have also found that the DNA encoding the PRO708 polypeptide has significant homology with DNA encoding the aryl sulfatase proteins. Accordingly, it is presently believed that PRO708 polypeptide disclosed in the present application is a newly identified aryl sulfatase homolog.

#### 18. Full-length PRO320 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO320. In particular, Applicants have identified and isolated cDNA encoding a PRO320 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO320 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO320 polypeptide have significant homology to the fibulin

protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO320 amino acid sequence and the following Dayhoff sequences, human fibulin-2 precursor, designated "FBL2\_HUMAN", human fibulin-1 isoform a precursor, designated "FBLA\_HUMAN", ZK783.1 - Caenorhabditis elegans, designated "CELZK783\_1", human-notch2, designated "HSU77493\_1", Nel protein precursor - rattus norvegicus, designated "NEL\_RAT", Mus musculus cell surface protein, designated "D32210\_1", mouse (fragment) Notch B protein, designated "A49175", C50H2.3a - Caenorhabditis elegans, designated "CEC50H2\_3", MEC-9L - Caenorhabditis elegans, designated "CEU33933\_1", and Mus musculus notch 4, designated "10 MMMHC29N7\_2", thereby indicating that PRO320 may be a novel fibulin or fibulin-like protein. Accordingly, it is presently believed that PRO320 polypeptide disclosed in the present application is a newly identified member of the fibulin family and possesses biological activity typical of the fibulin family.

#### 19. Full-length PRO324 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO324. In particular, Applicants have identified and isolated cDNA encoding a PRO324 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO324 polypeptide has significant similarity to oxidoreductases. Accordingly, it is presently believed that PRO324 polypeptide disclosed in the present application is a newly identified oxidoreductase homolog.

#### 20. Full-length PRO351 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO351. In particular, Applicants have identified and isolated cDNA encoding a PRO351 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO351 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO351 polypeptide possess significant sequence similarity to the prostasin protein, thereby indicating that PRO351 may be a novel prostasin protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO351 amino acid sequence and the following Dayhoff sequences, "AC003965\_1", "CELC07G1\_7", "GEN12917", "HEPS\_HUMAN", "GEN14584", "MCT6\_MOUSE", "HSU75329\_1", "PLMN\_ERIEU", "TRYB\_HUMAN", and "P\_W22987". Accordingly, it is presently believed that PRO351 polypeptide disclosed in the present application is a newly identified member of the prostasin family and possesses properties and activities typical of the prostasin family.

#### 21. Full-length PRO352 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO352. In particular, Applicants have identified and isolated cDNA

encoding a PRO352 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO352 polypeptide has significant similarity to the butyrophilin protein. Accordingly, it is presently believed that PRO352 polypeptide disclosed in the present application is a newly identified butyrophilin homolog.

5                   22.     Full-length PRO381 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO381. In particular, Applicants have identified and isolated cDNA encoding a PRO381 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO381 polypeptide has significant similarity  
10 to immunophilin proteins. Accordingly, it is presently believed that PRO381 polypeptide disclosed in the present application is a newly identified FKBP immunophilin homolog.

                  23.     Full-length PRO386 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO386. In particular, Applicants have identified and isolated cDNA encoding a PRO386 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO386 polypeptide has significant similarity  
15 to the beta-2 subunit of a sodium channel protein. Accordingly, it is presently believed that PRO386 polypeptide disclosed in the present application is homolog of a beta-2 subunit of a sodium channel expressed in mammalian  
20 cells.

                  24.     Full-length PRO540 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO540. In particular, Applicants have identified and isolated cDNA encoding a PRO540 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino  
25 acid sequence of the full-length PRO540 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO540 polypeptide possess significant sequence similarity to the LCAT protein, thereby indicating that PRO540 may be a novel LCAT protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the  
30 PRO540 amino acid sequence and the following Dayhoff sequences, phosphatidylcholine-sterol acyltransferase, designated "LCAT\_HUMAN", hypothetical 75.4 kd protein, designated "YN84\_YEAST", *Bacillus licheniformis* esterase, designated "BLU35855\_1", macrotetrolide resistance protein - *Streptomyces*, designated "JH0655", T-cell receptor delta chain precursor, designated "C30583", Rhesus kringle 2, designated "P\_W07551", RAGE-1 ORF5, designated "HSU46191\_3", human Ig kappa chain VKIII-JK3, designated  
35 "HSU07466\_1", and *Alstroemeria inodora* reverse transcriptase, designated "ALI223606\_1". Accordingly, it is presently believed that PRO540 polypeptide disclosed in the present application is a newly identified member

of the LCAT protein family and possesses lipid transport capability typical of the LCAT family.

25. **Full-length PRO615 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO615. In particular, Applicants have identified and isolated cDNA  
5 encoding a PRO615 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO615 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO615 polypeptide possess significant sequence similarity to the human synaptogyrin protein, thereby indicating that PRO615 may be a novel synaptogyrin protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence  
10 similarity between the PRO615 amino acid sequence and the following Dayhoff sequences, "AF039085\_1", "RNU39549\_1", "CELT08A9\_8", "FSU62028\_1", "S73645", "Y348\_MYCPN", "AC000103\_5", "", "RT12\_LEITA", and "EBVLMP218\_1". Accordingly, it is presently believed that PRO615 polypeptide disclosed in the present application is a newly identified member of the synaptogyrin family and possesses activity and properties typical of the synaptogyrin family.

26. **Full-length PRO618 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO618. In particular, Applicants have identified and isolated cDNA  
20 encoding a PRO618 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO618 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO618 polypeptide possess significant sequence similarity to the enteropeptidase protein, thereby indicating that PRO618 may be a novel enteropeptidase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO618 amino acid sequence and the following Dayhoff sequences, "P\_W22987",  
25 "KAL\_HUMAN", "AC003965\_1", "GEN12917", "ENTK\_HUMAN", "FA11\_HUMAN", "HSU75329\_1", "P\_W22986", and "PLMN\_HORSE". Accordingly, it is presently believed that PRO618 polypeptide disclosed in the present application is a newly identified member of the enteropeptidase family and possesses catalytic activity typical of the enteropeptidase family.

30 27. **Full-length PRO719 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO719. In particular, Applicants have identified and isolated cDNA  
35 encoding a PRO719 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO719 polypeptide has significant similarity to the lipoprotein lipase H protein. Accordingly, it is presently believed that PRO719 polypeptide disclosed in the present application is a newly identified lipoprotein lipase H homolog.

**28. Full-length PRO724 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO724. In particular, Applicants have identified and isolated cDNA encoding a PRO724 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO724 polypeptide has significant similarity to the human low density lipoprotein (LDL) receptor protein. Accordingly, it is presently believed that PRO724 polypeptide disclosed in the present application is a newly identified LDL receptor homolog.

**29. Full-length PRO772 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO772. In particular, Applicants have identified and isolated cDNA encoding a PRO772 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO772 polypeptide has significant similarity to the human A4 protein. Accordingly, it is presently believed that PRO772 polypeptide disclosed in the present application is a newly identified A4 protein homolog.

**30. Full-length PRO852 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO852. In particular, Applicants have identified and isolated cDNA encoding a PRO852 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO852 polypeptide has significant similarity to various protease proteins. Accordingly, it is presently believed that PRO852 polypeptide disclosed in the present application is a newly identified protease enzyme homolog.

**31. Full-length PRO853 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO853. In particular, Applicants have identified and isolated cDNA encoding a PRO853 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO853 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO853 polypeptide possess significant sequence similarity to the reductase protein, thereby indicating that PRO853 may be a novel reductase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO853 amino acid sequence and the following Dayhoff sequences, "P\_W03198", "CEC15H11\_6", "MTV030\_12", "P\_W15759", "S42651", "ATAC00234314", "MTV022\_13", "SCU43704\_1", "CELE04F6\_7", and "ALFA\_1". Accordingly, it is presently believed that PRO853 polypeptide disclosed in the present application is a newly identified member of the reductase family and possesses the antioxidant enzymatic activity typical of the reductase family.



**32. Full-length PRO860 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO860. In particular, Applicants have identified and isolated cDNA encoding a PRO860 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO860 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO860 polypeptide possess significant sequence similarity to the neurofascin protein, thereby indicating that PRO860 may be a novel neurofascin. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO860 amino acid sequence and the following Dayhoff sequences, "AF040990\_1", "AF041053\_1", "CELZK377\_2", "RNU81035\_1", "D86983\_1", "S26180", "MMBIG2A\_1", "S46216", and "RNU68726\_1".

Accordingly, it is presently believed that PRO860 polypeptide disclosed in the present application is a newly identified member of the neurofascin family and possesses the cellular adhesion properties typical of the neurofascin family.

**33. Full-length PRO846 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO846. In particular, Applicants have identified and isolated cDNA encoding a PRO846 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO846 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO846 polypeptide possess significant sequence similarity to the CMRF35 protein, thereby indicating that PRO846 may be a novel CMRF35 protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO846 amino acid sequence and the following Dayhoff sequences, "CM35\_HUMAN", "AF035963\_1", "PIGR\_RABIT", "AF043724\_1", "RNU89744\_1", "A52091\_1", "S48841", "ELK06A9\_3", and "AF049588\_1".

Accordingly, it is presently believed that PRO846 polypeptide disclosed in the present application is a newly identified member of the CMRF35 protein family and possesses properties typical of the CMRF35 protein family.

**34. Full-length PRO862 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO862. In particular, Applicants have identified and isolated cDNA encoding a PRO862 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO862 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO862 polypeptide possess significant sequence similarity to the lysozyme protein, thereby indicating that PRO862 may be a novel lysozyme protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO862 amino acid sequence and the following Dayhoff sequences, "P\_P90343", and "LYC\_HUMAN".

Accordingly, it is presently believed that PRO862 polypeptide disclosed in the present application is a newly identified member of the lysozyme family and possesses catalytic activity typical of the lysozyme family.

35. **Full-length PRO864 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO864. In particular, Applicants have identified and isolated cDNA encoding a PRO864 polypeptide, as disclosed in further detail in the Examples below. Analysis of the amino acid sequence of the full-length PRO864 polypeptide using BLAST and FastA sequence alignment computer programs, suggests that various portions of the PRO864 polypeptide possess significant sequence similarity to the Wnt-4 protein, thereby indicating that PRO864 may be a novel Wnt-4 protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant sequence similarity between the PRO864 amino acid sequence and the following Dayhoff sequences, "WNT4\_MOUSE", "WNT3\_MOUSE", "WN5A\_HUMAN", "WN7B\_MOUSE", "WN3A\_MOUSE", "XLU66288\_1", "WN13\_HUMAN", "WN5B\_ORYLA", "WNT2\_MOUSE", and "WN7A\_MOUSE". Accordingly, it is presently believed that PRO864 polypeptide disclosed in the present application is a newly identified member of the Wnt-4 protein family and possesses properties typical of the Wnt-4 protein family.

36. **Full-length PRO792 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO792. In particular, Applicants have identified and isolated cDNA encoding a PRO792 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO792 polypeptide has significant similarity to the CD23 protein. Accordingly, it is presently believed that PRO792 polypeptide disclosed in the present application is a newly identified CD23 homolog.

37. **Full-length PRO866 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO866. In particular, Applicants have identified and isolated cDNA encoding a PRO866 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO866 polypeptide has significant similarity to various mindin and spondin proteins. Accordingly, it is presently believed that PRO866 polypeptide disclosed in the present application is a newly identified mindin/spondin homolog.

38. **Full-length PRO871 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO871. In particular, Applicants have identified and isolated cDNA encoding a PRO871 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA

sequence alignment computer programs, Applicants found that the PRO871 polypeptide has significant similarity to the CyP-60 protein. Accordingly, it is presently believed that PRO871 polypeptide disclosed in the present application is a newly identified member of the cyclophilin protein family and possesses activity typical of the cyclophilin protein family.

5                    39.    Full-length PRO873 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO873. In particular, Applicants have identified and isolated cDNA encoding a PRO873 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO873 polypeptide has significant similarity  
10 to a human liver carboxylesterase. Accordingly, it is presently believed that PRO873 polypeptide disclosed in the present application is a newly identified member of the carboxylesterase family and possesses enzymatic activity typical of the carboxylesterase family.

15                    40.    Full-length PRO940 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO940. In particular, Applicants have identified and isolated cDNA encoding a PRO940 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO940 polypeptide has significant similarity to CD33 and the OB binding protein-2. Accordingly, it is presently believed that PRO940 polypeptide disclosed  
20 in the present application is a newly CD33 and/or OB binding protein-2 homolog.

25                    41.    Full-length PRO941 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO941. In particular, Applicants have identified and isolated cDNA  
25 encoding a PRO941 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO941 polypeptide has significant similarity to one or more cadherin proteins. Accordingly, it is presently believed that PRO941 polypeptide disclosed in the present application is a newly identified cadherin homolog.

30                    42.    Full-length PRO944 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO944. In particular, Applicants have identified and isolated cDNA encoding a PRO944 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO944 polypeptide has significant similarity  
35 to the CPE-R cell surface protein. Accordingly, it is presently believed that PRO944 polypeptide disclosed in the present application is a newly identified CPE-R homolog.

**43. Full-length PRO983 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO983. In particular, Applicants have identified and isolated cDNA encoding a PRO983 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO983 polypeptide has significant similarity to the vesicle-associated protein, VAP-33. Accordingly, it is presently believed that PRO983 polypeptide disclosed in the present application is a newly identified member of the vesicle-associated membrane protein family and possesses activity typical of vesicle-associated membrane proteins.

**44. Full-length PRO1057 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1057. In particular, Applicants have identified and isolated cDNA encoding a PRO1057 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO1057 polypeptide has significant similarity to various protease proteins. Accordingly, it is presently believed that PRO1057 polypeptide disclosed in the present application is a newly identified protease homolog.

**45. Full-length PRO1071 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1071. In particular, Applicants have identified and isolated cDNA encoding a PRO1071 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO1071 polypeptide has significant similarity to the thrombospondin protein. Accordingly, it is presently believed that PRO1071 polypeptide disclosed in the present application is a newly identified thrombospondin homolog.

**46. Full-length PRO1072 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1072. In particular, Applicants have identified and isolated cDNA encoding a PRO1072 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO1072 polypeptide has significant similarity to various reductase proteins. Accordingly, it is presently believed that PRO1072 polypeptide disclosed in the present application is a newly identified member of the reductase protein family.

**47. Full-length PRO1075 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1075. In particular, Applicants have identified and isolated cDNA encoding a PRO1075 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and

FastA sequence alignment computer programs, Applicants found that the PRO1075 polypeptide has significant similarity to protein disulfide isomerase. Accordingly, it is presently believed that PRO1075 polypeptide disclosed in the present application is a newly identified member of the protein disulfide isomerase family and possesses activity typical of that family.

5                   48.     Full-length PRO181 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO181. In particular, Applicants have identified and isolated cDNA encoding a PRO181 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO181 polypeptide has significant similarity  
10 to the cornichon protein. Accordingly, it is presently believed that PRO181 polypeptide disclosed in the present application is a newly identified cornichon homolog.

                  49.     Full-length PRO195 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO195. In particular, Applicants have identified and isolated cDNA  
15 encoding a PRO195 polypeptide, as disclosed in further detail in the Examples below. The PRO195-encoding clone was isolated from a human fetal placenta library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. To Applicants present knowledge, the UNQ169 (DNA26847-1395) nucleotide sequence encodes a novel factor; using BLAST and FastA sequence alignment computer programs,  
20 no sequence identities to any known proteins were revealed.

                  50.     Full-length PRO865 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO865. In particular, Applicants have identified and isolated cDNA  
25 encoding a PRO865 polypeptide, as disclosed in further detail in the Examples below. The PRO865-encoding clone was isolated from a human fetal kidney library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. Thus, the PRO865-encoding clone may encode a secreted factor. To Applicants present knowledge, the UNQ434 (DNA53974-1401) nucleotide sequence encodes a novel factor; using BLAST and FastA sequence alignment computer programs, no sequence identities to any known proteins  
30 were revealed.

                  51.     Full-length PRO827 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO827. In particular, Applicants have identified and isolated cDNA  
35 encoding a PRO827 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO827 polypeptide has significant similarity

to VLA-2 and various other integrin proteins. Accordingly, it is presently believed that PRO827 polypeptide disclosed in the present application is a novel integrin protein or splice variant thereof.

**52. Full-length PRO1114 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1114. In particular, Applicants have identified and isolated cDNA encoding a PRO1114 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO1114 polypeptide has significant similarity to the cytokine receptor family of proteins. Accordingly, it is presently believed that PRO1114 polypeptide disclosed in the present application is a newly identified member of the cytokine receptor family of proteins and possesses activity typical of that family.

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1114 interferon receptor (UNQ557). In particular, cDNA encoding a PRO1114 interferon receptor polypeptide has been identified and isolated, as disclosed in further detail in the Examples below. It is noted that proteins produced in separate expression rounds may be given different PRO numbers but the UNQ number is unique for any given DNA and the encoded protein, and will not be changed. However, for sake of simplicity, in the present specification the protein encoded by DNA57033-1403 as well as all further native homologues and variants included in the foregoing definition of PRO1114 interferon receptor, will be referred to as "PRO1114 interferon receptor", regardless of their origin or mode of preparation.

Using the WU-BLAST2 sequence alignment computer program, it has been found that a full-length native sequence PRO1114 interferon receptor polypeptide (shown in Figure 142 and SEQ ID NO:352) has sequence identity with the other known interferon receptors. Accordingly, it is presently believed that PRO1114 interferon receptor possesses activity typical of other interferon receptors.

**53. Full-length PRO237 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO237. In particular, Applicants have identified and isolated cDNA encoding a PRO237 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO237 polypeptide has significant similarity to carbonic anhydrase. Accordingly, it is presently believed that PRO237 polypeptide disclosed in the present application is a newly identified carbonic anhydrase homolog.

**54. Full-length PRO541 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO541. In particular, Applicants have identified and isolated cDNA encoding a PRO541 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO541 polypeptide has significant similarity

to a trypsin inhibitor protein. Accordingly, it is presently believed that PRO541 polypeptide disclosed in the present application is a newly identified member of the trypsin inhibitor protein family.

**55. Full-length PRO273 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO273. In particular, Applicants have identified and isolated cDNA encoding a PRO273 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO273 polypeptide have significant sequence identity with various chemokines. Accordingly, it is presently believed that PRO273 polypeptide disclosed in the present application is a newly identified member of the chemokine family and possesses activity typical of the chemokine family.

**56. Full-length PRO701 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO701. In particular, Applicants have identified and isolated cDNA encoding a PRO701 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO701 polypeptide have significant homology with the neuroligins 1, 2 and 3 and esterases including carboxyesterases and acetylcholinesterases. Accordingly, it is presently believed that PRO701 polypeptide disclosed in the present application is a newly identified member of the neuroligin family and is involved in mediating recognition processes between neurons and/or functions as a cell adhesion molecule as is typical of neuroligins.

**57. Full-length PRO704 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO704. In particular, Applicants have identified and isolated cDNA encoding a PRO704 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO704 polypeptide have significant homology with the VIP36 and GP36b. Accordingly, it is presently believed that PRO704 polypeptide disclosed in the present application is a newly identified member of the vesicular integral membrane protein family and possesses the ability to bind to sugars and cycle between the plasma membrane and the Golgi typical of this family.

**58. Full-length PRO706 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO706. In particular, Applicants have identified and isolated cDNA encoding a PRO706 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO706 polypeptide have

sequence identity with the human prostatic acid phosphatase precursor and the human lysosomal acid phosphatase precursor. Accordingly, it is presently believed that PRO706 polypeptide disclosed in the present application is a newly identified member of the human prostatic acid phosphatase precursor family and possesses phosphatase typical of the acid phosphatase family.

5                   59.     **Full-length PRO707 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO707. In particular, Applicants have identified and isolated cDNA encoding a PRO707 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO707 polypeptide have  
10 significant homology with cadherins, particularly cadherin FIB3 found in fibroblasts. Accordingly, it is presently believed that PRO707 polypeptide disclosed in the present application is a newly identified member of the cadherin family and possesses cell interaction signaling typical of the cadherin family.

15                   60.     **Full-length PRO322 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO322. In particular, Applicants have identified and isolated cDNA encoding a PRO322 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO322 polypeptide have  
20 significant homology with human neuropsin, serine protease, neurosin and trypsinogen. Accordingly, it is presently believed that PRO322 polypeptide disclosed in the present application is a newly identified member of the serine protease family and possesses protease activity typical of this family. It is also believed that PRO322 is involved in hippocampal plasticity and is associated with extracellular matrix modifications and cell migrations.

25                   61.     **Full-length PRO526 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO526. In particular, Applicants have identified and isolated cDNA encoding a PRO526 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO526 polypeptide have  
30 significant homology with the acid labile subunit of the insulin-like growth factor complex (ALS), as well carboxypeptidase, SLIT, and platelet glycoprotein V. Accordingly, it is presently believed that PRO526 polypeptide disclosed in the present application is a newly identified member of the leucine-repeat rich superfamily, and possesses protein-protein interaction capabilities typical of this family.

35                   62.     **Full-length PRO531 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides



referred to in the present application as PRO531. In particular, Applicants have identified and isolated cDNA encoding a PRO531 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO531 polypeptide have significant sequence identity and similarity with members of the cadherin superfamily, particularly, protocadherin 3. Accordingly, it is presently believed that PRO531 polypeptide disclosed in the present application is a newly identified member of the cadherin superfamily, and is a protocadherin. PRO531 is a transmembrane protein which has extracellular cadherin motifs. PRO531 is believed to be involved in cell-cell activity, in particular, cell signaling.

**63. Full-length PRO534 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO534. In particular, Applicants have identified and isolated cDNA encoding a PRO534 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO534 polypeptide have significant identity or similarity with the putative disulfide isomerase erp38 precursor and thioredoxin c-3. Accordingly, it is presently believed that PRO534 polypeptide disclosed in the present application is a newly identified member of the disulfide isomerase family and possesses the ability to recognize and unscramble either intermediate or incorrect folding patterns typical of this family.

**64. Full-length PRO697 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO697. In particular, Applicants have identified and isolated cDNA encoding a PRO697 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO697 polypeptide have significant identity or similarity with sFRP-2, sFRP-1 and SARP-1, -2 and -3. Accordingly, it is presently believed that PRO697 polypeptide disclosed in the present application is a newly identified member of the sFRP family and possesses activity related to the Wnt signal pathway.

**65. Full-length PRO717 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO717. In particular, Applicants have identified and isolated cDNA encoding a PRO717 polypeptide, as disclosed in further detail in the Examples below. To Applicants present knowledge, the UNQ385 (DNA50988-1326) nucleotide sequence encodes a novel factor; using BLAST and FastA sequence alignment computer programs, no significant sequence identities to any known human proteins were revealed.

**66. Full-length PRO731 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides

referred to in the present application as PRO731. In particular, Applicants have identified and isolated cDNA encoding a PRO731 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO731 polypeptide have significant homology with the protocadherins 4, 68, 43, 42, 3, and 5. Accordingly, it is presently believed that PRO731 polypeptide disclosed in the present application is a newly identified member of the protocadherin family and possesses cell-cell aggregation or signaling activity or signal transduction involvement typical of this family.

**67. Full-length PRO218 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO218. In particular, Applicants have identified and isolated cDNA encoding a PRO218 polypeptide, as disclosed in further detail in the Examples below. The PRO218-encoding clone was isolated from a human fetal kidney library. To Applicants present knowledge, the UNQ192 (DNA30867-1335) nucleotide sequence encodes a novel factor; using BLAST and FastA sequence alignment computer programs, no significant sequence identities to any known proteins were revealed. Some sequence identity was found with membrane regulator proteins, indicating that PRO218 may function as a membrane regulator.

**68. Full-length PRO768 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO768. In particular, Applicants have identified and isolated cDNA encoding a PRO768 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO768 polypeptide have significant homology with integrins, including integrin 7 and 6. Accordingly, it is presently believed that PRO768 polypeptide disclosed in the present application is a newly identified member of the integrin family, either a homologue or a splice variant of integrin 7, and is involved with cell adhesion and communication between muscle cells and the extracellular matrix.

**69. Full-length PRO771 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO771. In particular, Applicants have identified and isolated cDNA encoding a PRO771 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO771 polypeptide have significant sequence identity and similarity with testican. Accordingly, it is presently believed that PRO771 polypeptide disclosed in the present application is a newly identified member of the testican family and possesses cell signaling, binding, or adhesion properties, typical of this family.

70. Full-length PRO733 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO733. In particular, Applicants have identified and isolated cDNA encoding a PRO733 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO733 polypeptide have significant sequence identity with the T1/ST receptor binding protein. Accordingly, it is presently believed that PRO733 polypeptide disclosed in the present application is a newly identified member of the interleukin-like family binding proteins which may be a cytokine and which may be involved in cell signaling. It is believed that PRO733 is an ApoAIV homologue.

71. Full-length PRO162 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO162. In particular, Applicants have identified and isolated cDNA encoding a PRO162 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO162 polypeptide have significant homology with human pancreatitis-associated protein (PAP). Applicants have also found that the DNA encoding the PRO162 polypeptide has significant homology with bovine lithostathine precursor and bovine pancreatic thread protein (PTP). Accordingly, it is presently believed that PRO162 polypeptide disclosed in the present application is a newly identified member of the pancreatitis-associated protein family and possesses activity typical of the pancreatitis-associated protein family.

72. Full-length PRO788 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO788. In particular, Applicants have identified and isolated cDNA encoding a PRO788 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO788 polypeptide have significant homology with the anti-neoplastic urinary protein. Applicants have also found that the DNA encoding the PRO788 polypeptide has significant homology with human E48 antigen, human component B protein, and human prostate stem cell antigen. Accordingly, it is presently believed that PRO788 polypeptide disclosed in the present application is a newly identified member of the anti-neoplastic urinary protein family and possesses anti-neoplastic activity typical of the anti-neoplastic urinary protein family.

73. Full-length PRO1008 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1008. In particular, Applicants have identified and isolated cDNA encoding a PRO1008 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO1008

polypeptide have significant sequence identity and similarity with mouse dkk-1 (mdkk-1). Accordingly, it is presently believed that PRO1008 polypeptide disclosed in the present application is a newly identified member of the dkk-1 family and possesses head inducing activity typical of this family.

**74. Full-length PRO1012 Polypeptides**

5 The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1012. In particular, Applicants have identified and isolated cDNA encoding a PRO1012 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO1012 polypeptide have sequence identity with disulfide isomerase. Accordingly, it is presently believed that PRO1012  
10 polypeptide disclosed in the present application is a newly identified member of the ER retained protein family and possesses activity related to the processing, production and/or folding of polypeptides typical of the disulfide isomerase family.

**75. Full-length PRO1014 Polypeptides**

15 The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1014. In particular, Applicants have identified and isolated cDNA encoding a PRO1014 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO1014 polypeptide have sequence identity with reductase and dehydrogenase. Accordingly, it is presently believed that  
20 PRO1014 polypeptide disclosed in the present application is a newly identified member of the reductase super family and possesses reduction capabilities typical of this family.

**76. Full-length PRO1017 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides  
25 referred to in the present application as PRO1017. In particular, Applicants have identified and isolated cDNA encoding a PRO1017 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO1017 polypeptide have sequence identity with HNK-1 sulfotransferase. Accordingly, it is presently believed that PRO1017 polypeptide disclosed in the present application is a newly identified member of the HNK-1  
30 sulfotransferase family and is involved with the synthesis of HNK-1 carbohydrate epitopes typical of this family.

**77. Full-length PRO474 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO474. In particular, Applicants have identified and isolated cDNA  
35 encoding a PRO474 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO474 polypeptide have

sequence identity with dehydrogenase, glucose dehydrogenase and oxidoreductase. Accordingly, it is presently believed that PRO474 polypeptide disclosed in the present application is a newly identified member of the dehydrogenase family and is involved in the oxidation of glucose.

**78. Full-length PRO1031 Polypeptides**

5 The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1031. In particular, Applicants have identified and isolated cDNA encoding a PRO1031 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO1031 polypeptide have sequence identity with IL-17 and CTLA-8. Accordingly, it is presently believed that PRO1031  
10 polypeptide disclosed in the present application is a newly identified member of the cytokine family and thus may be involved in inflammation and/or the immune system.

**79. Full-length PRO938 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO938. In particular, Applicants have identified and isolated cDNA  
15 encoding a PRO938 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the PRO938 polypeptide has significant similarity to protein disulfide isomerase. Accordingly, it is presently believed that PRO938 polypeptide disclosed in the present application is a newly identified member of the thioredoxin family proteins and possesses activity typical  
20 of protein disulfide isomerase.

**80. Full-length PRO1082 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1082. In particular, Applicants have identified and isolated cDNA  
25 encoding a PRO1082 polypeptide, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that various portions of the PRO1082 polypeptide have sequence identity with a lectin-like oxidized LDL receptor appearing in the database as "AB010710\_1". Accordingly, it is presently believed that PRO1082 polypeptide disclosed in the present application is a newly identified member of the LDL receptor family.  
30

**81. Full-length PRO1083 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO1083. In particular, Applicants have identified and isolated cDNA encoding a PRO1083 polypeptide, as disclosed in further detail in the Examples below. The PRO1083-encoding  
35 clone was isolated from a human fetal kidney library using a trapping technique which selects for nucleotide sequences encoding secreted proteins. To Applicants present knowledge, the UNQ540 (DNA50921-1458)

nucleotide sequence encodes a novel factor; using BLAST and FastA sequence alignment computer programs, some sequence identity with a 7TM receptor, latrophilin related protein 1 and a macrophage restricted cell surface glycoprotein was shown. The kinase phosphorylation site and G-coupled receptor domain shown in Figure 204 indicate that PRO1083 is a novel member of the 7TM receptor superfamily.

5                    **82.     Full-length PRO200 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as VEGF-E. In particular, Applicants have identified and isolated cDNA encoding a VEGF-E polypeptide, as disclosed in further detail in the Examples below. Using BLAST sequence alignment computer programs, Applicants found that the VEGF-E polypeptide has significant homology with VEGF and bone morphogenetic protein 1. In particular, the cDNA sequence of VEGF-E exhibits 24 % amino acid similarity with VEGF and has structural conservation. In addition, VEGF-E contains a N-terminal half which is not present in VEGF and that has 28 % homology to bone morphogenetic protein 1.

15                    **83.     Full-length PRO285 and PRO286 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO285 and PRO286. In particular, Applicants have identified and isolated cDNAs encoding PRO285 and PRO286 polypeptides, as disclosed in further detail in the Examples below. Using BLAST and FastA sequence alignment computer programs, Applicants found that the coding sequences of PRO285 and PRO286 are highly homologous to DNA sequences HSU88540\_1, HSU88878\_1, HSU88879\_1, HSU88880\_1, and HSU88881\_1 in the GenBank database.

Accordingly, it is presently believed that the PRO285 and PRO286 proteins disclosed in the present application are newly identified human homologues of the *Drosophila* protein Toll, and are likely to play an important role in adaptive immunity. More specifically, PRO285 and PRO286 may be involved in inflammation, septic shock, and response to pathogens, and play possible roles in diverse medical conditions that are aggravated by immune response, such as, for example, diabetes, ALS, cancer, rheumatoid arthritis, and ulcers. The role of PRO285 and PRO286 as pathogen pattern recognition receptors, sensing the presence of conserved molecular structures present on microbes, is further supported by the data disclosed in the present application, showing that a known human Toll-like receptor, TLR2 is a direct mediator of LPS signaling.

30                    **84.     Full-length PRO213-1, PRO1330 and PRO1449 Polypeptides**

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO213-1, PRO1330 and/or PRO1449. In particular, cDNA encoding a PRO213-1, PRO1330 and/or PRO1449 polypeptide has been identified and isolated, as disclosed in further detail in the Examples below. It is noted that proteins produced in separate expression rounds may be given different PRO numbers but the UNQ number is unique for any given DNA and the encoded protein, and will not be changed. However, for sake of simplicity, in the present specification the protein encoded by DNA30943-

1163-1, DNA64907-1163-1 and DNA64908-1163-1 as well as all further native homologues and variants included in the foregoing definition of PRO213-1, PRO1330 and/or PRO1449, will be referred to as "PRO213-1, PRO1330 and/or PRO1449", regardless of their origin or mode of preparation.

#### 85. Full-length PRO298 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO298. (It is noted that PRO298 is an arbitrary designation of a protein encoded by the nucleic acid shown in Figure 218, SEQ ID NO: 514, and having the amino acid sequence shown in Figure 219, SEQ ID NO:515. Further proteins having the same amino acid sequence but expressed in different rounds of expression, may be given different "PRO" numbers.)

In particular, Applicants have identified and isolated cDNA encoding a PRO298 polypeptide, as disclosed in further detail in the Examples below. Using BLASTX 2.0a8MP-WashU computer program, socring parameters: T=12, S=68, S2=36, Matrix: BLOSUM62, Applicants found that the PRO298 protein specifically disclosed herein shows a limited (27-38%) sequence identity with the following sequences found in the GenBank database: S59392 (probable membrane protein YLR246w - yeast); S58154 (hypothetical protein SPAC2F7.10 - yeast); CELF33D11\_9 (F33D11.9b - *Caenorhabditis elegans*); YO41\_CAEEL (hypothetical 68.7 kd protein zk757.1); CEAC3\_5 (AC3.4 - *Caenorhabditis elegans*); S52691 (probable transmembrane protein YDR126w - yeast); ATT12H17\_14 (protein - *Arabidopsis thaliana*); S55963 (probable membrane protein YNL326c - yeast); CELC43H6\_2 (C43H6.7 - *Caenorhabditis elegans*); TMO18A10\_14 (A\_TMO18A10.8 - *Arabinosa thaliana*).

#### 86. Full-length PRO337 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO337. In particular, Applicants have identified and isolated cDNA encoding a PRO337 polypeptide, as disclosed in further detail in the Examples below. Using BLAST, BLAST-2 and FastA sequence alignment computer programs, Applicants found that a full-length native sequence PRO337 has 97% amino acid sequence identity with rat neurotrimin, 85% sequence identity with chicken CEPU, 73% sequence identity with chicken G55, 59% homology with human LAMP and 84% homology with human OPCAM. Accordingly, it is presently believed that PRO337 disclosed in the present application is a newly identified member of the IgLON sub family of the immunoglobulin superfamily and may possess neurite growth and differentiation potentiating properties.

#### 87. Full-length PRO403 Polypeptides

The present invention provides newly identified and isolated nucleotide sequences encoding polypeptides referred to in the present application as PRO403. In particular, Applicants have identified and isolated cDNA encoding a PRO403 polypeptide, as disclosed in further detail in the Examples below. Using a BLAST, BLAST-2 and FastA sequence alignment computer programs, Applicants found that a full-length native sequence PRO403 has 94% identity to bovine ECE-2 and 64% identity to human ECE-1. Accordingly is presently believed that

PRO403 is a new member of the ECE protein family and may possess ability to catalyze the production of active endothelin.

#### 88. PRO Polypeptide Variants

In addition to the full-length native sequence PRO polypeptides described herein, it is contemplated that PRO polypeptide variants can be prepared. PRO polypeptide variants can be prepared by introducing appropriate nucleotide changes into the PRO polypeptide DNA, or by synthesis of the desired PRO polypeptide. Those skilled in the art will appreciate that amino acid changes may alter post-translational processes of the PRO polypeptides, such as changing the number or position of glycosylation sites or altering the membrane anchoring characteristics.

Variations in the native full-length sequence PRO polypeptides or in various domains of the PRO polypeptides described herein, can be made, for example, using any of the techniques and guidelines for conservative and non-conservative mutations set forth, for instance, in U.S. Patent No. 5,364,934. Variations may be a substitution, deletion or insertion of one or more codons encoding the PRO polypeptide that results in a change in the amino acid sequence of the PRO polypeptide as compared with the native sequence PRO polypeptide. Optionally the variation is by substitution of at least one amino acid with any other amino acid in one or more of the domains of the PRO polypeptide. Guidance in determining which amino acid residue may be inserted, substituted or deleted without adversely affecting the desired activity may be found by comparing the sequence of the PRO polypeptide with that of homologous known protein molecules and minimizing the number of amino acid sequence changes made in regions of high homology. Amino acid substitutions can be the result of replacing one amino acid with another amino acid having similar structural and/or chemical properties, such as the replacement of a leucine with a serine, i.e., conservative amino acid replacements. Insertions or deletions may optionally be in the range of 1 to 5 amino acids. The variations allowed may be determined by systematically making insertions, deletions or substitutions of amino acids in the sequence and testing the resulting variants for activity in the *in vitro* assay described in the Examples below.

In particular embodiments, conservative substitutions of interest are shown in Table 1 under the heading of preferred substitutions. If such substitutions result in a change in biological activity, then more substantial changes, denominated exemplary substitutions in Table 1, or as further described below in reference to amino acid classes, are introduced and the products screened.



Table 1

	<u>Original Residue</u>	<u>Exemplary Substitutions</u>	<u>Preferred Substitutions</u>
5	Ala (A)	val; leu; ile	val
	Arg (R)	lys; gln; asn	lys
	Asn (N)	gln; his; lys; arg	gln
	Asp (D)	glu	glu
	Cys (C)	ser	ser
10	Gln (Q)	asn	asn
	Glu (E)	asp	asp
	Gly (G)	pro; ala	ala
	His (H)	asn; gln; lys; arg	arg
	Ile (I)	leu; val; met; ala; phe;	
15		norleucine	leu
	Leu (L)	norleucine; ile; val;	
		met; ala; phe	ile
	Lys (K)	arg; gln; asn	arg
	Met (M)	leu; phe; ile	leu
20	Phe (F)	leu; val; ile; ala; tyr	leu
	Pro (P)	ala	ala
	Ser (S)	thr	thr
	Thr (T)	ser	ser
	Trp (W)	tyr; phe	tyr
25	Tyr (Y)	trp; phe; thr; ser	phe
	Val (V)	ile; leu; met; phe;	
		ala; norleucine	leu

Substantial modifications in function or immunological identity of the PRO polypeptide are accomplished by selecting substitutions that differ significantly in their effect on maintaining (a) the structure of the polypeptide backbone in the area of the substitution, for example, as a sheet or helical conformation, (b) the charge or hydrophobicity of the molecule at the target site, or (c) the bulk of the side chain. Naturally occurring residues are divided into groups based on common side-chain properties:

- (1) hydrophobic: norleucine, met, ala, val, leu, ile;
- (2) neutral hydrophilic: cys, ser, thr;
- (3) acidic: asp, glu;
- (4) basic: asn, gln, his, lys, arg;
- (5) residues that influence chain orientation: gly, pro; and
- (6) aromatic: trp, tyr, phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class. Such substituted residues also may be introduced into the conservative substitution sites or, more preferably, into the remaining (non-conserved) sites.

The variations can be made using methods known in the art such as oligonucleotide-mediated (site-directed) mutagenesis, alanine scanning, and PCR mutagenesis. Site-directed mutagenesis [Carter et al., Nucl. Acids Res., 13:4331 (1986); Zoller et al., Nucl. Acids Res., 10:6487 (1987)], cassette mutagenesis [Wells et

al., Gene, 34:315 (1985)], restriction selection mutagenesis [Wells et al., Philos. Trans. R. Soc. London SerA, 317:415 (1986)] or other known techniques can be performed on the cloned DNA to produce the desired PRO polypeptide variant DNA.

Scanning amino acid analysis can also be employed to identify one or more amino acids along a contiguous sequence. Among the preferred scanning amino acids are relatively small, neutral amino acids. Such amino acids include alanine, glycine, serine, and cysteine. Alanine is typically a preferred scanning amino acid among this group because it eliminates the side-chain beyond the beta-carbon and is less likely to alter the main-chain conformation of the variant. Alanine is also typically preferred because it is the most common amino acid. Further, it is frequently found in both buried and exposed positions [Creighton, The Proteins, (W.H. Freeman & Co., N.Y.); Chothia, J. Mol. Biol., 150:1 (1976)]. If alanine substitution does not yield adequate amounts of variant, an isoteric amino acid can be used.

#### 89. Modifications of PRO Polypeptides

Covalent modifications of PRO polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of the PRO polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N- or C- terminal residues of the PRO polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking a PRO polypeptide to a water-insoluble support matrix or surface for use in the method for purifying anti-PRO polypeptide antibodies, and vice-versa. Commonly used crosslinking agents include, *e.g.*, 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, for example, esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-[(p-azidophenyl)-dithio]propionimidate.

Other modifications include deamidation of glutamyl and asparaginy residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of seryl or threonyl residues, methylation of the  $\alpha$ -amino groups of lysine, arginine, and histidine side chains [T.E. Creighton, Proteins: Structure and Molecular Properties, W.H. Freeman & Co., San Francisco, pp. 79-86 (1983)], acetylation of the N-terminal amine, and amidation of any C-terminal carboxyl group.

Another type of covalent modification of the PRO polypeptides included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in a native sequence PRO polypeptide, and/or adding one or more glycosylation sites that are not present in the native sequence PRO polypeptide, and/or alteration of the ratio and/or composition of the sugar residues attached to the glycosylation site(s).

Addition of glycosylation sites to the PRO polypeptide may be accomplished by altering the amino acid sequence. The alteration may be made, for example, by the addition of, or substitution by, one or more serine or threonine residues to the native sequence PRO polypeptide (for O-linked glycosylation sites). The PRO

polypeptide amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the PRO polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the PRO polypeptide polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330 published 11 September 1987, and in Aplin and Wriston, CRC Crit. Rev. Biochem., pp. 259-306 (1981).

Removal of carbohydrate moieties present on the PRO polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, for instance, by Hakimuddin, et al., Arch. Biochem. Biophys., 259:52 (1987) and by Edge et al., Anal. Biochem., 118:131 (1981). Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo- and exo-glycosidases as described by Thotakura et al., Meth. Enzymol., 138:350 (1987).

Another type of covalent modification of PRO polypeptides of the invention comprises linking the PRO polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192 or 4,179,337.

The PRO polypeptides of the present invention may also be modified in a way to form a chimeric molecule comprising a PRO polypeptide fused to another, heterologous polypeptide or amino acid sequence. In one embodiment, such a chimeric molecule comprises a fusion of the PRO polypeptide with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino- or carboxyl- terminus of the PRO polypeptide. The presence of such epitope-tagged forms of the PRO polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the PRO polypeptide to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. In an alternative embodiment, the chimeric molecule may comprise a fusion of the PRO polypeptide with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule, such a fusion could be to the Fc region of an IgG molecule.

Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; the flu HA tag polypeptide and its antibody 12CA5 [Field et al., Mol. Cell. Biol., 8:2159-2165 (1988)]; the c-myc tag and the 8F9, 3C7, 6E10, G4, B7 and 9E10 antibodies thereto [Evan et al., Molecular and Cellular Biology, 5:3610-3616 (1985)]; and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody [Paborsky et al., Protein Engineering, 3(6):547-553 (1990)]. Other tag polypeptides include the Flag-peptide [Hopp et al., BioTechnology, 6:1204-1210 (1988)]; the KT3 epitope peptide [Martin et al., Science, 255:192-194 (1992)]; an  $\alpha$ -tubulin epitope peptide [Skinner et al., J. Biol. Chem., 266:15163-15166 (1991)]; and the T7 gene 10 protein peptide tag [Lutz-Freyermuth et al., Proc. Natl. Acad. Sci. USA, 87:6393-6397 (1990)].

## 90. Preparation of PRO Polypeptides

The description below relates primarily to production of PRO polypeptides by culturing cells transformed or transfected with a vector containing the desired PRO polypeptide nucleic acid. It is, of course, contemplated that alternative methods, which are well known in the art, may be employed to prepare the PRO polypeptide. For instance, the PRO polypeptide sequence, or portions thereof, may be produced by direct peptide synthesis using solid-phase techniques [see, e.g., Stewart et al., Solid-Phase Peptide Synthesis, W.H. Freeman Co., San Francisco, CA (1969); Merrifield, J. Am. Chem. Soc., 85:2149-2154 (1963)]. *In vitro* protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be accomplished, for instance, using an Applied Biosystems Peptide Synthesizer (Foster City, CA) using manufacturer's instructions. Various portions of the desired PRO polypeptide may be chemically synthesized separately and combined using chemical or enzymatic methods to produce the full-length PRO polypeptide.

### A. Isolation of DNA Encoding PRO Polypeptides

DNA encoding PRO polypeptides may be obtained from a cDNA library prepared from tissue believed to possess the desired PRO polypeptide mRNA and to express it at a detectable level. Accordingly, human PRO polypeptide DNA can be conveniently obtained from a cDNA library prepared from human tissue, such as described in the Examples. The PRO polypeptide-encoding gene may also be obtained from a genomic library or by oligonucleotide synthesis.

Libraries can be screened with probes (such as antibodies to the desired PRO polypeptide or oligonucleotides of at least about 20-80 bases) designed to identify the gene of interest or the protein encoded by it. Screening the cDNA or genomic library with the selected probe may be conducted using standard procedures, such as described in Sambrook et al., Molecular Cloning: A Laboratory Manual (New York: Cold Spring Harbor Laboratory Press, 1989). An alternative means to isolate the gene encoding the desired PRO polypeptide is to use PCR methodology [Sambrook et al., *supra*; Dieffenbach et al., PCR Primer: A Laboratory Manual (Cold Spring Harbor Laboratory Press, 1995)].

The Examples below describe techniques for screening a cDNA library. The oligonucleotide sequences selected as probes should be of sufficient length and sufficiently unambiguous that false positives are minimized. The oligonucleotide is preferably labeled such that it can be detected upon hybridization to DNA in the library being screened. Methods of labeling are well known in the art, and include the use of radiolabels like <sup>32</sup>P-labeled ATP, biotinylation or enzyme labeling. Hybridization conditions, including moderate stringency and high stringency, are provided in Sambrook et al., *supra*.

Sequences identified in such library screening methods can be compared and aligned to other known sequences deposited and available in public databases such as GenBank or other private sequence databases. Sequence identity (at either the amino acid or nucleotide level) within defined regions of the molecule or across the full-length sequence can be determined through sequence alignment using computer software programs such as BLAST, ALIGN, DNASTAR, and INHERIT which employ various algorithms to measure homology.

Nucleic acid having protein coding sequence may be obtained by screening selected cDNA or genomic

libraries using the deduced amino acid sequence disclosed herein for the first time, and, if necessary, using conventional primer extension procedures as described in Sambrook et al., supra, to detect precursors and processing intermediates of mRNA that may not have been reverse-transcribed into cDNA.

#### B. Selection and Transformation of Host Cells

5 Host cells are transfected or transformed with expression or cloning vectors described herein for PRO polypeptide production and cultured in conventional nutrient media modified as appropriate for inducing promoters, selecting transformants, or amplifying the genes encoding the desired sequences. The culture conditions, such as media, temperature, pH and the like, can be selected by the skilled artisan without undue experimentation. In general, principles, protocols, and practical techniques for maximizing the productivity of  
10 cell cultures can be found in Mammalian Cell Biotechnology: a Practical Approach, M. Butler, ed. (IRL Press, 1991) and Sambrook et al., supra.

Methods of transfection are known to the ordinarily skilled artisan, for example,  $\text{CaPO}_4$  and electroporation. Depending on the host cell used, transformation is performed using standard techniques appropriate to such cells. The calcium treatment employing calcium chloride, as described in Sambrook et al.,  
15 supra, or electroporation is generally used for prokaryotes or other cells that contain substantial cell-wall barriers. Infection with *Agrobacterium tumefaciens* is used for transformation of certain plant cells, as described by Shaw et al., Gene, 23:315 (1983) and WO 89/05859 published 29 June 1989. For mammalian cells without such cell walls, the calcium phosphate precipitation method of Graham and van der Eb, Virology, 52:456-457 (1978) can be employed. General aspects of mammalian cell host system transformations have been described  
20 in U.S. Patent No. 4,399,216. Transformations into yeast are typically carried out according to the method of Van Solingen et al., J. Bact., 130:946 (1977) and Hsiao et al., Proc. Natl. Acad. Sci. (USA), 76:3829 (1979). However, other methods for introducing DNA into cells, such as by nuclear microinjection, electroporation, bacterial protoplast fusion with intact cells, or polycations, e.g., polybrene, polyornithine, may also be used. For various techniques for transforming mammalian cells, see Keown et al., Methods in Enzymology, 185:527-  
25 537 (1990) and Mansour et al., Nature, 336:348-352 (1988).

Suitable host cells for cloning or expressing the DNA in the vectors herein include prokaryote, yeast, or higher eukaryote cells. Suitable prokaryotes include but are not limited to eubacteria, such as Gram-negative or Gram-positive organisms, for example, Enterobacteriaceae such as *E. coli*. Various *E. coli* strains are publicly available, such as *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli*  
30 strain W3110 (ATCC 27,325) and K5 772 (ATCC 53,635). Other suitable prokaryotic host cells include Enterobacteriaceae such as *Escherichia*, e.g., *E. coli*, *Enterobacter*, *Erwinia*, *Klebsiella*, *Proteus*, *Salmonella*, e.g., *Salmonella typhimurium*, *Serratia*, e.g., *Serratia marcescans*, and *Shigella*, as well as *Bacilli* such as *B. subtilis* and *B. licheniformis* (e.g., *B. licheniformis* 41P disclosed in DD 266,710 published 12 April 1989), *Pseudomonas* such as *P. aeruginosa*, and *Streptomyces*. Various *E. coli* strains are publicly available, such as  
35 *E. coli* K12 strain MM294 (ATCC 31,446); *E. coli* X1776 (ATCC 31,537); *E. coli* strain W3110 (ATCC 27,325); and K5 772 (ATCC 53,635). These examples are illustrative rather than limiting. Strain W3110 is

one particularly preferred host or parent host because it is a common host strain for recombinant DNA product fermentations. Preferably, the host cell secretes minimal amounts of proteolytic enzymes. For example, strain W3110 may be modified to effect a genetic mutation in the genes encoding proteins endogenous to the host, with examples of such hosts including *E. coli* W3110 strain 1A2, which has the complete genotype *tonA*; *E. coli* W3110 strain 9E4, which has the complete genotype *tonA ptr3*; *E. coli* W3110 strain 27C7 (ATCC 55,244), which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT kan'*; *E. coli* W3110 strain 37D6, which has the complete genotype *tonA ptr3 phoA E15 (argF-lac)169 degP ompT rbs7 ilvG kan'*; *E. coli* W3110 strain 40B4, which is strain 37D6 with a non-kanamycin resistant *degP* deletion mutation; and an *E. coli* strain having mutant periplasmic protease disclosed in U.S. Patent No. 4,946,783 issued 7 August 1990. Alternatively, *in vitro* methods of cloning, e.g., PCR or other nucleic acid polymerase reactions, are suitable.

In addition to prokaryotes, eukaryotic microbes such as filamentous fungi or yeast are suitable cloning or expression hosts for PRO polypeptide-encoding vectors. *Saccharomyces cerevisiae* is a commonly used lower eukaryotic host microorganism. Others include *Schizosaccharomyces pombe* (Beach and Nurse, Nature, 290: 140 [1981]; EP 139,383 published 2 May 1985); *Kluyveromyces* hosts (U.S. Patent No. 4,943,529; Fleer *et al.*, Bio/Technology, 9: 968-975 (1991)) such as, e.g., *K. lacris* (MW98-8C, CBS683, CBS4574; Louvencourt *et al.*, J. Bacteriol., 737 [1983]), *K. fragilis* (ATCC 12,424), *K. bulgaricus* (ATCC 16,045), *K. wickerhamii* (ATCC 24,178), *K. waltii* (ATCC 56,500), *K. drosophilum* (ATCC 36,906; Van den Berg *et al.*, Bio/Technology, 8: 135 (1990)), *K. thermotolerans*, and *K. marxianus*; *Yarrowia* (EP 402,226); *Pichia pastoris* (EP 183,070; Sreekrishna *et al.*, J. Basic Microbiol., 28: 265-278 [1988]); *Candida*; *Trichoderma reesia* (EP 244,234); *Neurospora crassa* (Case *et al.*, Proc. Natl. Acad. Sci. USA, 76: 5259-5263 [1979]); *Schwanniomyces* such as *Schwanniomyces occidentalis* (EP 394,538 published 31 October 1990); and filamentous fungi such as, e.g., *Neurospora*, *Penicillium*, *Totipocladium* (WO 91/00357 published 10 January 1991), and *Aspergillus* hosts such as *A. nidulans* (Ballance *et al.*, Biochem. Biophys. Res. Commun., 112: 284-289 [1983]; Tilburn *et al.*, Gene, 26: 205-221 [1983]; Yelton *et al.*, Proc. Natl. Acad. Sci. USA, 81: 1470-1474 [1984]) and *A. niger* (Kelly and Hynes, EMBO J., 4: 475-479 [1985]). Methylotropic yeasts are suitable herein and include, but are not limited to, yeast capable of growth on methanol selected from the genera consisting of *Hansenula*, *Candida*, *Kloeckera*, *Pichia*, *Saccharomyces*, *Torulopsis*, and *Rhodotorula*. A list of specific species that are exemplary of this class of yeasts may be found in C. Anthony, The Biochemistry of Methylotrophs, 269 (1982).

Suitable host cells for the expression of glycosylated PRO polypeptides are derived from multicellular organisms. Examples of invertebrate cells include insect cells such as *Drosophila* S2 and *Spodoptera* Sf9, as well as plant cells. Examples of useful mammalian host cell lines include Chinese hamster ovary (CHO) and COS cells. More specific examples include monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham *et al.*, J. Gen. Virol., 36:59 (1977)); Chinese hamster ovary cells/-DHFR (CHO, Urlaub and Chasin, Proc. Natl. Acad. Sci. USA, 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod., 23:243-251 (1980)); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); and mouse mammary tumor (MMT 060562, ATCC CCL51). The selection of the appropriate host cell is deemed to be within the skill in the art.

### C. Selection and Use of a Replicable Vector

The nucleic acid (*e.g.*, cDNA or genomic DNA) encoding a desired PRO polypeptide may be inserted into a replicable vector for cloning (amplification of the DNA) or for expression. Various vectors are publicly available. The vector may, for example, be in the form of a plasmid, cosmid, viral particle, or phage. The appropriate nucleic acid sequence may be inserted into the vector by a variety of procedures. In general, DNA is inserted into an appropriate restriction endonuclease site(s) using techniques known in the art. Vector components generally include, but are not limited to, one or more of a signal sequence, an origin of replication, one or more marker genes, an enhancer element, a promoter, and a transcription termination sequence. Construction of suitable vectors containing one or more of these components employs standard ligation techniques which are known to the skilled artisan.

The PRO polypeptide of interest may be produced recombinantly not only directly, but also as a fusion polypeptide with a heterologous polypeptide, which may be a signal sequence or other polypeptide having a specific cleavage site at the N-terminus of the mature protein or polypeptide. In general, the signal sequence may be a component of the vector, or it may be a part of the PRO polypeptide DNA that is inserted into the vector. The signal sequence may be a prokaryotic signal sequence selected, for example, from the group of the alkaline phosphatase, penicillinase, lpp, or heat-stable enterotoxin II leaders. For yeast secretion the signal sequence may be, *e.g.*, the yeast invertase leader, alpha factor leader (including *Saccharomyces* and *Kluyveromyces*  $\alpha$ -factor leaders, the latter described in U.S. Patent No. 5,010,182), or acid phosphatase leader, the *C. albicans* glucoamylase leader (EP 362,179 published 4 April 1990), or the signal described in WO 90/13646 published 15 November 1990. In mammalian cell expression, mammalian signal sequences may be used to direct secretion of the protein, such as signal sequences from secreted polypeptides of the same or related species, as well as viral secretory leaders.

Both expression and cloning vectors contain a nucleic acid sequence that enables the vector to replicate in one or more selected host cells. Such sequences are well known for a variety of bacteria, yeast, and viruses. The origin of replication from the plasmid pBR322 is suitable for most Gram-negative bacteria, the 2 $\mu$  plasmid origin is suitable for yeast, and various viral origins (SV40, polyoma, adenovirus, VSV or BPV) are useful for cloning vectors in mammalian cells.

Expression and cloning vectors will typically contain a selection gene, also termed a selectable marker. Typical selection genes encode proteins that (a) confer resistance to antibiotics or other toxins, *e.g.*, ampicillin, neomycin, methotrexate, or tetracycline, (b) complement auxotrophic deficiencies, or (c) supply critical nutrients not available from complex media, *e.g.*, the gene encoding D-alanine racemase for *Bacilli*.

An example of suitable selectable markers for mammalian cells are those that enable the identification of cells competent to take up the PRO polypeptide nucleic acid, such as DHFR or thymidine kinase. An appropriate host cell when wild-type DHFR is employed is the CHO cell line deficient in DHFR activity, prepared and propagated as described by Urlaub et al., *Proc. Natl. Acad. Sci. USA*, **77**:4216 (1980). A suitable selection gene for use in yeast is the *trp1* gene present in the yeast plasmid YRp7 [Stinchcomb et al., *Nature*, **282**:39 (1979); Kingsman et al., *Gene*, **7**:141 (1979); Tschemper et al., *Gene*, **10**:157 (1980)]. The *trp1* gene

provides a selection marker for a mutant strain of yeast lacking the ability to grow in tryptophan, for example, ATCC No. 44076 or PEP4-1 [Jones, Genetics, 85:12 (1977)].

Expression and cloning vectors usually contain a promoter operably linked to the PRO polypeptide nucleic acid sequence to direct mRNA synthesis. Promoters recognized by a variety of potential host cells are well known. Promoters suitable for use with prokaryotic hosts include the  $\beta$ -lactamase and lactose promoter systems [Chang et al., Nature, 275:615 (1978); Goeddel et al., Nature, 281:544 (1979)], alkaline phosphatase, a tryptophan (trp) promoter system [Goeddel, Nucleic Acids Res., 8:4057 (1980); EP 36,776], and hybrid promoters such as the tac promoter [deBoer et al., Proc. Natl. Acad. Sci. USA, 80:21-25 (1983)]. Promoters for use in bacterial systems also will contain a Shine-Dalgarno (S.D.) sequence operably linked to the DNA encoding the desired PRO polypeptide.

Examples of suitable promoting sequences for use with yeast hosts include the promoters for 3-phosphoglycerate kinase [Hitzeman et al., J. Biol. Chem., 255:2073 (1980)] or other glycolytic enzymes [Hess et al., J. Adv. Enzyme Reg., 7:149 (1968); Holland, Biochemistry, 17:4900 (1978)], such as enolase, glyceraldehyde-3-phosphate dehydrogenase, hexokinase, pyruvate decarboxylase, phosphofructokinase, glucose-6-phosphate isomerase, 3-phosphoglycerate mutase, pyruvate kinase, triosephosphate isomerase, phosphoglucose isomerase, and glucokinase.

Other yeast promoters, which are inducible promoters having the additional advantage of transcription controlled by growth conditions, are the promoter regions for alcohol dehydrogenase 2, isocytochrome C, acid phosphatase, degradative enzymes associated with nitrogen metabolism, metallothionein, glyceraldehyde-3-phosphate dehydrogenase, and enzymes responsible for maltose and galactose utilization. Suitable vectors and promoters for use in yeast expression are further described in EP 73,657.

PRO polypeptide transcription from vectors in mammalian host cells is controlled, for example, by promoters obtained from the genomes of viruses such as polyoma virus, fowlpox virus (UK 2,211,504 published 5 July 1989), adenovirus (such as Adenovirus 2), bovine papilloma virus, avian sarcoma virus, cytomegalovirus, a retrovirus, hepatitis-B virus and Simian Virus 40 (SV40), from heterologous mammalian promoters, e.g., the actin promoter or an immunoglobulin promoter, and from heat-shock promoters, provided such promoters are compatible with the host cell systems.

Transcription of a DNA encoding the desired PRO polypeptide by higher eukaryotes may be increased by inserting an enhancer sequence into the vector. Enhancers are cis-acting elements of DNA, usually about from 10 to 300 bp, that act on a promoter to increase its transcription. Many enhancer sequences are now known from mammalian genes (globin, elastase, albumin,  $\alpha$ -fetoprotein, and insulin). Typically, however, one will use an enhancer from a eukaryotic cell virus. Examples include the SV40 enhancer on the late side of the replication origin (bp 100-270), the cytomegalovirus early promoter enhancer, the polyoma enhancer on the late side of the replication origin, and adenovirus enhancers. The enhancer may be spliced into the vector at a position 5' or 3' to the PRO polypeptide coding sequence, but is preferably located at a site 5' from the promoter.

Expression vectors used in eukaryotic host cells (yeast, fungi, insect, plant, animal, human, or nucleated cells from other multicellular organisms) will also contain sequences necessary for the termination of



transcription and for stabilizing the mRNA. Such sequences are commonly available from the 5' and, occasionally 3', untranslated regions of eukaryotic or viral DNAs or cDNAs. These regions contain nucleotide segments transcribed as polyadenylated fragments in the untranslated portion of the mRNA encoding PRO polypeptides.

5 Still other methods, vectors, and host cells suitable for adaptation to the synthesis of PRO polypeptides in recombinant vertebrate cell culture are described in Gething et al., Nature, 293:620-625 (1981); Mantei et al., Nature, 281:40-46 (1979); EP 117,060; and EP 117,058.

#### D. Detecting Gene Amplification/Expression

Gene amplification and/or expression may be measured in a sample directly, for example, by  
10 conventional Southern blotting, Northern blotting to quantitate the transcription of mRNA [Thomas, Proc. Natl. Acad. Sci. USA, 77:5201-5205 (1980)], dot blotting (DNA analysis), or *in situ* hybridization, using an appropriately labeled probe, based on the sequences provided herein. Alternatively, antibodies may be employed that can recognize specific duplexes, including DNA duplexes, RNA duplexes, and DNA-RNA hybrid duplexes or DNA-protein duplexes. The antibodies in turn may be labeled and the assay may be carried out where the  
15 duplex is bound to a surface, so that upon the formation of duplex on the surface, the presence of antibody bound to the duplex can be detected.

Gene expression, alternatively, may be measured by immunological methods, such as immunohistochemical staining of cells or tissue sections and assay of cell culture or body fluids, to quantitate directly the expression of gene product. Antibodies useful for immunohistochemical staining and/or assay of  
20 sample fluids may be either monoclonal or polyclonal, and may be prepared in any mammal. Conveniently, the antibodies may be prepared against a native sequence PRO polypeptide or against a synthetic peptide based on the DNA sequences provided herein or against exogenous sequence fused to a PRO polypeptide DNA and encoding a specific antibody epitope.

#### 25 E. Purification of Polypeptide

Forms of PRO polypeptides may be recovered from culture medium or from host cell lysates. If membrane-bound, it can be released from the membrane using a suitable detergent solution (*e.g.* Triton-X 100) or by enzymatic cleavage. Cells employed in expression of PRO polypeptides can be disrupted by various physical or chemical means, such as freeze-thaw cycling, sonication, mechanical disruption, or cell lysing agents.

30 It may be desired to purify PRO polypeptides from recombinant cell proteins or polypeptides. The following procedures are exemplary of suitable purification procedures: by fractionation on an ion-exchange column; ethanol precipitation; reverse phase HPLC; chromatography on silica or on a cation-exchange resin such as DEAE; chromatofocusing; SDS-PAGE; ammonium sulfate precipitation; gel filtration using, for example, Sephadex G-75; protein A Sepharose columns to remove contaminants such as IgG; and metal chelating columns  
35 to bind epitope-tagged forms of the PRO polypeptide. Various methods of protein purification may be employed and such methods are known in the art and described for example in Deutscher, Methods in Enzymology, 182

(1990); Scopes, Protein Purification: Principles and Practice, Springer-Verlag, New York (1982). The purification step(s) selected will depend, for example, on the nature of the production process used and the particular PRO polypeptide produced.

#### 91. Uses for PRO Polypeptides

5 Nucleotide sequences (or their complement) encoding the PRO polypeptides of the present invention have various applications in the art of molecular biology, including uses as hybridization probes, in chromosome and gene mapping and in the generation of anti-sense RNA and DNA. PRO polypeptide-encoding nucleic acid will also be useful for the preparation of PRO polypeptides by the recombinant techniques described herein.

The full-length native sequence PRO polypeptide-encoding nucleic acid or portions thereof, may be used  
10 as hybridization probes for a cDNA library to isolate the full-length PRO polypeptide gene or to isolate still other genes (for instance, those encoding naturally-occurring variants of the PRO polypeptide or PRO polypeptides from other species) which have a desired sequence identity to the PRO polypeptide nucleic acid sequences. Optionally, the length of the probes will be about 20 to about 50 bases. The hybridization probes may be derived from the nucleotide sequence of any of the DNA molecules disclosed herein or from genomic sequences  
15 including promoters, enhancer elements and introns of native sequence PRO polypeptide encoding DNA. By way of example, a screening method will comprise isolating the coding region of the PRO polypeptide gene using the known DNA sequence to synthesize a selected probe of about 40 bases. Hybridization probes may be labeled by a variety of labels, including radionucleotides such as <sup>32</sup>P or <sup>35</sup>S, or enzymatic labels such as alkaline phosphatase coupled to the probe via avidin/biotin coupling systems. Labeled probes having a sequence  
20 complementary to that of the specific PRO polypeptide gene of the present invention can be used to screen libraries of human cDNA, genomic DNA or mRNA to determine which members of such libraries the probe hybridizes to. Hybridization techniques are described in further detail in the Examples below.

The ESTs disclosed in the present application may similarly be employed as probes, using the methods disclosed herein.

25 The probes may also be employed in PCR techniques to generate a pool of sequences for identification of closely related PRO polypeptide sequences.

Nucleotide sequences encoding a PRO polypeptide can also be used to construct hybridization probes for mapping the gene which encodes that PRO polypeptide and for the genetic analysis of individuals with genetic disorders. The nucleotide sequences provided herein may be mapped to a chromosome and specific regions of  
30 a chromosome using known techniques, such as *in situ* hybridization, linkage analysis against known chromosomal markers, and hybridization screening with libraries.

When the coding sequence for the PRO polypeptide encodes a protein which binds to another protein, the PRO polypeptide can be used in assays to identify its ligands. Similarly, inhibitors of the receptor/ligand binding interaction can be identified. Proteins involved in such binding interactions can also be used to screen  
35 for peptide or small molecule inhibitors or agonists of the binding interaction. Screening assays can be designed to find lead compounds that mimic the biological activity of a native PRO polypeptide or a ligand for the PRO

polypeptide. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic or inorganic compounds. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the art.

- 5 Nucleic acids which encode a PRO polypeptide or its modified forms can also be used to generate either transgenic animals or "knock out" animals which, in turn, are useful in the development and screening of therapeutically useful reagents. A transgenic animal (e.g., a mouse or rat) is an animal having cells that contain a transgene, which transgene was introduced into the animal or an ancestor of the animal at a prenatal, e.g., an embryonic stage. A transgene is a DNA which is integrated into the genome of a cell from which a transgenic
- 10 animal develops. In one embodiment, cDNA encoding a PRO polypeptide of interest can be used to clone genomic DNA encoding the PRO polypeptide in accordance with established techniques and the genomic sequences used to generate transgenic animals that contain cells which express DNA encoding the PRO polypeptide. Methods for generating transgenic animals, particularly animals such as mice or rats, have become conventional in the art and are described, for example, in U.S. Patent Nos. 4,736,866 and 4,870,009.
- 15 Typically, particular cells would be targeted for PRO polypeptide transgene incorporation with tissue-specific enhancers. Transgenic animals that include a copy of a transgene encoding a PRO polypeptide introduced into the germ line of the animal at an embryonic stage can be used to examine the effect of increased expression of DNA encoding the PRO polypeptide. Such animals can be used as tester animals for reagents thought to confer protection from, for example, pathological conditions associated with its overexpression. In accordance with
- 20 this facet of the invention, an animal is treated with the reagent and a reduced incidence of the pathological condition, compared to untreated animals bearing the transgene, would indicate a potential therapeutic intervention for the pathological condition.

- Alternatively, non-human homologues of PRO polypeptides can be used to construct a PRO polypeptide "knock out" animal which has a defective or altered gene encoding the PRO polypeptide of interest as a result
- 25 of homologous recombination between the endogenous gene encoding the PRO polypeptide and altered genomic DNA encoding the PRO polypeptide introduced into an embryonic cell of the animal. For example, cDNA encoding a PRO polypeptide can be used to clone genomic DNA encoding the PRO polypeptide in accordance with established techniques. A portion of the genomic DNA encoding a PRO polypeptide can be deleted or replaced with another gene, such as a gene encoding a selectable marker which can be used to monitor
- 30 integration. Typically, several kilobases of unaltered flanking DNA (both at the 5' and 3' ends) are included in the vector [see e.g., Thomas and Capecchi, *Cell*, 51:503 (1987) for a description of homologous recombination vectors]. The vector is introduced into an embryonic stem cell line (e.g., by electroporation) and cells in which the introduced DNA has homologously recombined with the endogenous DNA are selected [see e.g., Li et al., *Cell*, 69:915 (1992)]. The selected cells are then injected into a blastocyst of an animal (e.g.,
- 35 a mouse or rat) to form aggregation chimeras [see e.g., Bradley, in *Teratocarcinomas and Embryonic Stem Cells: A Practical Approach*, E. J. Robertson, ed. (IRL, Oxford, 1987), pp. 113-152]. A chimeric embryo can

then be implanted into a suitable pseudopregnant female foster animal and the embryo brought to term to create a "knock out" animal. Progeny harboring the homologously recombined DNA in their germ cells can be identified by standard techniques and used to breed animals in which all cells of the animal contain the homologously recombined DNA. Knockout animals can be characterized for instance, for their ability to defend against certain pathological conditions and for their development of pathological conditions due to absence of the PRO polypeptide.

When *in vivo* administration of a PRO polypeptide is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1 µg/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 4,657,760; 5,206,344; or 5,225,212.

It is anticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a manner different from that to another organ or tissue.

Where sustained-release administration of a PRO polypeptide is desired in a formulation with release characteristics suitable for the treatment of any disease or disorder requiring administration of the PRO polypeptide, microencapsulation of the PRO polypeptide is contemplated. Microencapsulation of recombinant proteins for sustained release has been successfully performed with human growth hormone (rhGH), interferon-(rhIFN-), interleukin-2, and MN rgp120. Johnson *et al.*, Nat. Med., 2: 795-799 (1996); Yasuda, Biomed. Ther., 27: 1221-1223 (1993); Hora *et al.*, Bio/Technology, 8: 755-758 (1990); Cleland, "Design and Production of Single Immunization Vaccines Using Polylactide Polyglycolide Microsphere Systems," in Vaccine Design: The Subunit and Adjuvant Approach, Powell and Newman, eds, (Plenum Press: New York, 1995), pp. 439-462; WO 97/03692, WO 96/40072, WO 96/07399; and U.S. Pat. No. 5,654,010.

The sustained-release formulations of these proteins were developed using poly-lactic-co-glycolic acid (PLGA) polymer due to its biocompatibility and wide range of biodegradable properties. The degradation products of PLGA, lactic and glycolic acids, can be cleared quickly within the human body. Moreover, the degradability of this polymer can be adjusted from months to years depending on its molecular weight and composition. Lewis, "Controlled release of bioactive agents from lactide/glycolide polymer," in: M. Chasin and R. Langer (Eds.), Biodegradable Polymers as Drug Delivery Systems (Marcel Dekker: New York, 1990), pp. 1-41.

For example, for a formulation that can provide a dosing of approximately 80 g/kg/day in mammals with a maximum body weight of 85 kg, the largest dosing would be approximately 6.8 mg of the PRO polypeptide per day. In order to achieve this dosing level, a sustained-release formulation which contains a maximum possible protein loading (15-20% w/w PRO polypeptide) with the lowest possible initial burst (<20%) is necessary. A continuous (zero-order) release of the PRO polypeptide from microparticles for 1-2 weeks is also desirable. In addition, the encapsulated protein to be released should maintain its integrity and stability over the desired release period.

PRO213 polypeptides and portions thereof which possess the ability to regulate the growth induction

cascade and/or the blood coagulation cascade may also be employed for such purposes both *in vivo* therapy and *in vitro*. Those of ordinary skill in the art will well know how to employ PRO213 polypeptides for such uses.

PRO274 polypeptides and portions thereof which have homology to 7TM protein and Fn54 may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel 7TM protein and Fn54-like molecules may have relevance to a number of human disorders which involve  
5 recognition of ligands and the subsequent signal transduction of information contained within those ligands in order to control cellular processes. Thus, the identification of new 7TM protein and Fn54-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as in various industrial applications. As a result, there is particular scientific and medical interest in new molecules,  
10 such as PRO274.

PRO300 polypeptides and portions thereof which have homology to Diff 33 may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel Diff 33-like molecules may have relevance to a number of human disorders such as the physiology of cancer. Thus, the identification of new Diff 33-like molecules is of special importance in that such proteins may serve as potential  
15 therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO300.

PRO296 polypeptides of the present invention which possess biological activity related to that of the sarcoma-amplified SAS protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of  
20 ordinary skill in the art will well know how to employ the PRO296 polypeptides of the present invention for such purposes.

~~PRO329 polypeptides of the present invention which possess biological activity related to that of~~  
immunoglobulin F<sub>c</sub> receptor protein or subunit thereof may be employed both *in vivo* for therapeutic purposes  
and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO329 polypeptides of the  
25 present invention for such purposes.

PRO362 polypeptides of the present invention which possess biological activity related to that of the A33 antigen protein, HCAR protein or the NrCAM related cell adhesion molecule may be employed both *in vivo* for therapeutic purposes and *in vitro*.

PRO363 polypeptides of the present invention which possess biological activity related to that of the cell  
30 surface HCAR protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO363 polypeptides of the present invention for such purposes. Specifically, extracellular domains derived from the PRO363 polypeptides may be employed therapeutically *in vivo* for lessening the effects of viral infection.

PRO868 polypeptides of the present invention which possess biological activity related to that of the  
35 tumor necrosis factor protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO868 polypeptides of the present invention for such

purposes.

PRO382 polypeptides of the present invention which possess biological activity related to that of the serine protease proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO382 polypeptides of the present invention for such purposes.

5 PRO545 polypeptides and portions thereof which have homology to meltrin may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel molecules associated with cellular adhesion may be relevant to a number of human disorders. Given that the meltrin proteins may play an important role in a number of disease processes, the identification of new meltrin proteins and meltrin-like molecules is of special importance in that such proteins may serve as potential therapeutics for  
10 a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research, as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO545.

PRO617 polypeptides of the present invention which possess biological activity related to that of the CD24 protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in  
15 the art will well know how to employ the PRO617 polypeptides of the present invention for such purposes.

PRO700 polypeptides and portions thereof which have homology to protein disulfide isomerase may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel protein disulfide isomerases and related molecules may be relevant to a number of human disorders. Given that formation of disulfide bonds and protein folding play important roles in a number of biological processes,  
20 the identification of new protein disulfide isomerases and protein disulfide isomerase-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research, as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO700.

25 PRO702 polypeptides of the present invention which possess biological activity related to that of the conglutinin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO702 polypeptides of the present invention for such purposes. PRO702 polypeptides having conglutinin activity would be expected to be capable of inhibiting haemagglutinin activity by influenza viruses and/or function as immunoglobulin-independent defense molecules as a result of  
30 a complement-mediated mechanism.

PRO703 polypeptides of the present invention which possess biological activity related to that of the VLCAS protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO703 polypeptides of the present invention for such purposes.

35 PRO703 polypeptides and portions thereof which have homology to VLCAS may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel VLCAS proteins and related molecules may be relevant to a number of human disorders. Thus, the identification of new VLCAS

proteins and VLCAS protein-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO703.

5 PRO705 polypeptides of the present invention which possess biological activity related to that of the K-glypican protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO705 polypeptides of the present invention for such purposes.

PRO708 polypeptides of the present invention which possess biological activity related to that of the aryl sulfatase proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO708 polypeptides of the present invention for such purposes.

10 PRO320 polypeptides of the present invention which possess biological activity related to that of the fibulin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO320 polypeptides of the present invention for such purposes.

PRO320 polypeptides and portions thereof which have homology to fibulin may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel fibulin proteins and related molecules may be relevant to a number of human disorders such as cancer or those involving connective tissue, attachment molecules and related mechanisms. Thus, the identification of new fibulin proteins and fibulin protein-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO320.

PRO324 polypeptides of the present invention which possess biological activity related to that of oxidoreductases may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO324 polypeptides of the present invention for such purposes.

25 PRO351 polypeptides of the present invention which possess biological activity related to that of the prostatic protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO351 polypeptides of the present invention for such purposes.

PRO351 polypeptides and portions thereof which have homology to prostatic protein may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel prostatic proteins and related molecules may be relevant to a number of human disorders. Thus, the identification of new prostatic proteins and prostatic -like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO351.

35 PRO352 polypeptides of the present invention which possess biological activity related to that of the butyrophilin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO352 polypeptides of the present invention for such purposes.

PRO381 polypeptides of the present invention which possess biological activity related to that of one or more of the FKBP immunophilin proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*, for example for enhancing immunosuppressant activity and/or for axonal regeneration. Those of ordinary skill in the art will well know how to employ the PRO381 polypeptides of the present invention for such purposes.

5 PRO386 polypeptides of the present invention which possess biological activity related to that of the beta-2 subunit of a sodium channel expressed in mammalian cells may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO386 polypeptides of the present invention for such purposes.

10 PRO540 polypeptides of the present invention which possess biological activity related to that of the LCAT protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO540 polypeptides of the present invention for such purposes.

PRO615 polypeptides of the present invention which possess biological activity related to that of the synaptogyrin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO615 polypeptides of the present invention for such purposes.

15 PRO615 polypeptides and portions thereof which have homology to synaptogyrin may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel synaptogyrin proteins and related molecules may be relevant to a number of human disorders. Thus, the identification of new synaptogyrin proteins and synaptogyrin-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications. As  
20 a result, there is particular scientific and medical interest in new molecules, such as PRO615.

PRO618 polypeptides of the present invention which possess biological activity related to that of an enteropeptidase may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO618 polypeptides of the present invention for such purposes.

25 PRO618 polypeptides and portions thereof which have homology to enteropeptidase may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel enteropeptidase proteins and related molecules may be relevant to a number of human disorders. Thus, the identification of new enteropeptidase proteins and enteropeptidase-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications.  
30 As a result, there is particular scientific and medical interest in new molecules, such as PRO618.

PRO719 polypeptides of the present invention which possess biological activity related to that of the lipoprotein lipase H protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO719 polypeptides of the present invention for such purposes.

35 PRO724 polypeptides of the present invention which possess biological activity related to that of the human LDL receptor protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of



ordinary skill in the art will well know how to employ the PRO724 polypeptides of the present invention for such purposes.

PRO772 polypeptides of the present invention which possess biological activity related to that of the human A4 protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO772 polypeptides of the present invention for such purposes.

5 PRO852 polypeptides of the present invention which possess biological activity related to that of certain protease protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO852 polypeptides of the present invention for such purposes.

PRO853 polypeptides of the present invention which possess biological activity related to that of the reductase protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill  
10 in the art will well know how to employ the PRO853 polypeptides of the present invention for such purposes.

PRO853 polypeptides and portions thereof which have homology to reductase proteins may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. Given that oxygen free radicals and antioxidants appear to play important roles in a number of disease processes, the identification of new reductase proteins and reductase-like molecules is of special importance in that such proteins may serve as  
15 potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO853.

PRO860 polypeptides of the present invention which possess biological activity related to that of the neurofascin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill  
20 in the art will well know how to employ the PRO860 polypeptides of the present invention for such purposes.

PRO860 polypeptides and portions thereof which have homology to neurofascin may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel neurofascin proteins and related molecules may be relevant to a number of human disorders which involve cellular adhesion. Thus, the identification of new neurofascin proteins and neurofascin protein-like molecules is of special  
25 importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO860.

PRO846 polypeptides of the present invention which possess biological activity related to that of the CMRF35 protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill  
30 in the art will well know how to employ the PRO846 polypeptides of the present invention for such purposes.

PRO846 polypeptides and portions thereof which have homology to the CMRF35 protein may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel CMRF35 protein and related molecules may be relevant to a number of human disorders. Thus, the  
35 identification of new CMRF35 protein and CMRF35 protein-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may

also play important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO846.

PRO862 polypeptides of the present invention which possess biological activity related to that of the lysozyme protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO862 polypeptides of the present invention for such purposes.

5 PRO862 polypeptides and portions thereof which have homology to the lysozyme protein may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel lysozyme proteins and related molecules may be relevant to a number of human disorders. Thus, the identification of new lysozymes and lysozyme-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play  
10 important roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO862.

PRO864 polypeptides of the present invention which possess biological activity related to that of the Wnt-4 protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO864 polypeptides of the present invention for such purposes.

15 PRO864 polypeptides and portions thereof which have homology to the Wnt-4 protein may also be useful for *in vivo* therapeutic purposes, as well as for various other applications. The identification of novel Wnt-4 proteins and related molecules may be relevant to a number of human disorders. Thus, the identification of new Wnt-4 protein and Wnt-4 protein-like molecules is of special importance in that such proteins may serve as potential therapeutics for a variety of different human disorders. Such polypeptides may also play important  
20 roles in biotechnological and medical research as well as various industrial applications. As a result, there is particular scientific and medical interest in new molecules, such as PRO864.

PRO792 polypeptides of the present invention which possess biological activity related to that of the CD23 protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO792 polypeptides of the present invention for such purposes.

25 PRO866 polypeptides of the present invention which possess biological activity related to that of mindin and/or spondin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO866 polypeptides of the present invention for such purposes.

PRO871 polypeptides of the present invention which possess biological activity related to that of the cyclophilin protein family may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO871 polypeptides of the present invention for such purposes.

PRO873 polypeptides of the present invention which possess biological activity related to that of carboxylesterases may be employed both *in vivo* for therapeutic purposes and *in vitro*. For example, they be  
35 used in conjunction with prodrugs to convert the prodrug to its active form (see Danks *et al., supra*). They may be used to inhibit parasite infection (see van Pelt *et al., supra*). Methods for employ the PRO873 polypeptides

of the present invention for these, and other purposes will be readily apparent to those of ordinary skill in the art.

PRO940 polypeptides of the present invention which possess biological activity related to that of the CD33 protein and/or OB binding protein-2 may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO940 polypeptides of the present invention for such purposes.

PRO941 polypeptides of the present invention which possess biological activity related to that of a cadherin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO941 polypeptides of the present invention for such purposes.

PRO944 polypeptides of the present invention which possess biological activity related to that of the CPE-R protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO944 polypeptides of the present invention for such purposes. PRO944 polypeptides of the present invention that function to bind to Clostridium perfringens enterotoxin (CPE) may find use for effectively treating infection by the CPE endotoxin.

PRO983 polypeptides of the present invention which possess biological activity related to that of the vesicle-associated membrane protein, VAP-33, may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO983 polypeptides of the present invention for such purposes.

PRO1057 polypeptides of the present invention which possess biological activity related to that of protease proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1057 polypeptides of the present invention for such purposes.

PRO1071 polypeptides of the present invention which possess biological activity related to that of the thrombospondin protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1071 polypeptides of the present invention for such purposes.

PRO1072 polypeptides of the present invention which possess biological activity related to that of reductase proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1072 polypeptides of the present invention for such purposes.

PRO1075 polypeptides of the present invention which possess biological activity related to that of protein disulfide isomerase may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1075 polypeptides of the present invention for such purposes.

PRO181 polypeptides of the present invention which possess biological activity related to that of the cornichon protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO181 polypeptides of the present invention for such purposes.

PRO827 polypeptides of the present invention which possess biological activity related to that of various integrin proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill

in the art will well know how to employ the PRO827 polypeptides of the present invention for such purposes.

PRO1114 polypeptides of the present invention which possess biological activity related to that of the cytokine receptor family of proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1114 polypeptides of the present invention for such purposes.

5 In addition to the above, the PRO1114 interferon receptor polypeptides may be employed in applications, both *in vivo* and *in vitro*, where the ability to bind to an interferon ligand is desired. Such applications will be well within the skill level in the art.

PRO237 polypeptides of the present invention which possess biological activity related to that of the carbonic anhydrase protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of  
10 ordinary skill in the art will well know how to employ the PRO237 polypeptides of the present invention for such purposes.

PRO541 polypeptides of the present invention which possess biological activity related to that of a trypsin inhibitor protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO541 polypeptides of the present invention for such  
15 purposes.

PRO273 polypeptides can be used in assays that other chemokines would be used in to perform comparative assays. The results can be used accordingly.

PRO701 polypeptides of the present invention which possess biological activity related to that of the neuroligin family may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill  
20 in the art will well know how to employ the PRO701 polypeptides of the present invention for such purposes.

PRO701 can be used in assays with neurons and its activity thereon can be compared with that of neurons 1, 2 and 3. The results can be applied accordingly.

PRO704 polypeptides of the present invention which possess biological activity related to that of vesicular integral membrane proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those  
25 of ordinary skill in the art will well know how to employ the PRO704 polypeptides of the present invention for such purposes.

PRO704 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly. PRO704 can be tagged or measured for activity to measure endocytosis activity and thereby used to screen for agents which effect endocytosis.

30 PRO706 polypeptides of the present invention which possess biological activity related to that of the endogenous prostatic acid phosphatase precursor may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO706 polypeptides of the present invention for such purposes.

PRO706 can be used in assays with human prostatic acid phosphatase or human lysosomal acid  
35 phosphatase and its activity thereon can be compared with that of human prostatic acid phosphatase or human lysosomal acid phosphatase. The results can be applied accordingly.

PRO707 polypeptides of the present invention which possess biological activity related to that of cadherins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO707 polypeptides of the present invention for such purposes.

PRO707 can be used in assays to determine its activity in relation to other cadherins, particularly cadherin FIB3. The results can be applied accordingly.

5 PRO322 polypeptides of the present invention which possess biological activity related to that of neuropsin may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO322 polypeptides of the present invention for such purposes.

PRO322 can be used in assays to determine its activity relative to neuropsin, trypsinogen, serine protease and neurosin, and the results applied accordingly.

10 PRO526 polypeptides of the present invention which possess biological activity related to that of protein-protein binding proteins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO526 polypeptides of the present invention for such purposes.

Assays can be performed with growth factors and other proteins which are known to form complexes to determine whether PRO526 binds thereto and whether there is increased half-life due to such binding. The results can be used accordingly.

PRO531 polypeptides of the present invention which possess biological activity related to that of the protocadherins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO531 polypeptides of the present invention for such purposes.

20 PRO531 can be used in assays against protocadherin 3 and other protocadherins, to determine their relative activities. The results can be applied accordingly.

~~PRO534 polypeptides of the present invention which possess biological activity related to that of an~~  
protein disulfide isomerase may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO534 polypeptides of the present invention for such purposes.

25 PRO534 can be used in assays with protein disulfide isomerase to determine the relative activities. The results can be applied accordingly.

PRO697 polypeptides of the present invention which possess biological activity related to that of the sFRP family may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO697 polypeptides of the present invention for such purposes.

30 PRO697 can be used in assays with sFRPs and SARPs to determine the relative activities. The results can be applied accordingly.

PRO731 polypeptides of the present invention which possess biological activity related to that of any protocadherin may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO731 polypeptides of the present invention for such purposes.

PRO731 can be used in assays with the polypeptides to which they have identity with to determine the

relative activities. The results can be applied accordingly.

PRO768 polypeptides of the present invention which possess biological activity related to that of integrins may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO768 polypeptides of the present invention for such purposes.

5 PRO768 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO771 polypeptides of the present invention which possess biological activity related to that of the testican protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO771 polypeptides of the present invention for such purposes.

10 PRO771 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO733 polypeptides of the present invention which possess biological activity related to that of the proteins which bind the T1/ST2 receptor may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO733 polypeptides of the present invention for such purposes.

15 PRO733 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO162 polypeptides of the present invention which possess biological activity related to that of the pancreatitis-associated protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO162 polypeptides of the present invention for such purposes.

20 PRO162 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO788 polypeptides of the present invention which possess biological activity related to that of the anti-neoplastic urinary protein may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO788 polypeptides of the present invention for such purposes.

25 PRO788 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO1008 polypeptides of the present invention which possess biological activity related to that of dkk-1 may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1008 polypeptides of the present invention for such purposes.

PRO1008 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

35 PRO1012 polypeptides of the present invention which possess biological activity related to that of the protein disulfide isomerase may be employed both *in vivo* and *in vitro* purposes. Those of ordinary skill in the art will well know how to employ the PRO1012 polypeptides of the present invention for such purposes.

PRO1012 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO1014 polypeptides of the present invention which possess biological activity related to that of reductase may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1014 polypeptides of the present invention for such purposes.

5 PRO1014 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. Inhibitors of PRO1014 are particularly preferred. The results can be applied accordingly.

PRO1017 polypeptides of the present invention which possess biological activity related to that of sulfotransferase may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1017 polypeptides of the present invention for such purposes.

10 PRO1017 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO474 polypeptides of the present invention which possess biological activity related to that of dehydrogenase may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO474 polypeptides of the present invention for such purposes.

15 PRO474 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO1031 polypeptides of the present invention which possess biological activity related to that of IL-17 may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1031 polypeptides of the present invention for such purposes.

20 PRO1031 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly.

PRO938 polypeptides of the present invention which possess biological activity related to that of protein disulfide isomerase may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO938 polypeptides of the present invention for such purposes.

25 PRO1082 polypeptides of the present invention which possess biological activity related to that of the LDL receptor may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1082 polypeptides of the present invention for such purposes.

PRO1082 can be used in assays with the polypeptides to which they have identity with to determine the relative activities. The results can be applied accordingly. PRO1082 can also be used in assays to identify  
30 candidate agents which modulate the receptors.

PRO1083 polypeptides of the present invention which possess biological activity related to that of 7TM receptors may be employed both *in vivo* for therapeutic purposes and *in vitro*. Those of ordinary skill in the art will well know how to employ the PRO1083 polypeptides of the present invention for such purposes.

In particular PRO1083 can be used in assays to determine candidate agents which control or modulate  
35 PRO1083, i.e., have an effect on the receptor.

The VEGF-E molecules herein have a number of therapeutic uses associated with survival, proliferation

and/or differentiation of cells. Such uses include the treatment of umbilical vein endothelial cells, in view of the demonstrated ability of VEGF-E to increase survival of human umbilical vein endothelial cells. Treatment may be needed if the vein were subjected to traumata, or situations wherein artificial means are employed to enhance the survival of the umbilical vein, for example, where it is weak, diseased, based on an artificial matrix, or in an artificial environment. Other physiological conditions that could be improved based on the selective mitogenic character of VEGF-E are also included herein. Uses also include the treatment of fibroblasts and myocytes, in view of the demonstrated ability of VEGF-E to induce proliferation of fibroblasts and hypertrophy in myocytes. In particular, VEGF-E can be used in wound healing, tissue growth and muscle generation and regeneration.

For the indications referred to above, the VEGF-E molecule will be formulated and dosed in a fashion consistent with good medical practice taking into account the specific disorder to be treated, the condition of the individual patient, the site of delivery of the VEGF-E, the method of administration, and other factors known to practitioners. Thus, for purposes herein, the "therapeutically effective amount" of the VEGF-E is an amount that is effective either to prevent, lessen the worsening of, alleviate, or cure the treated condition, in particular that amount which is sufficient to enhance the survival, proliferation and/or differentiation of the treated cells in vivo.

VEGF-E amino acid variant sequences and derivatives that are immunologically crossreactive with antibodies raised against native VEGF are useful in immunoassays for VEGF-E as standards, or, when labeled, as competitive reagents.

The VEGF-E is prepared for storage or administration by mixing VEGF-E having the desired degree of purity with physiologically acceptable carriers, excipients, or stabilizers. Such materials are non-toxic to recipients at the dosages and concentrations employed. If the VEGF-E is water soluble, it may be formulated in a buffer such as phosphate or other organic acid salt preferably at a pH of about 7 to 8. If the VEGF-E is only partially soluble in water, it may be prepared as a microemulsion by formulating it with a nonionic surfactant such as Tween, Pluronic, or PEG, e.g., Tween 80, in an amount of 0.04-0.05% (w/v), to increase its solubility.

Optionally other ingredients may be added such as antioxidants, e.g., ascorbic acid; low molecular weight (less than about ten residues) polypeptides, e.g., polyarginine or tripeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids, such as glycine, glutamic acid, aspartic acid, or arginine; monosaccharides, disaccharides, and other carbohydrates including cellulose or its derivatives, glucose, mannose, or dextrans; chelating agents such as EDTA; and sugar alcohols such as mannitol or sorbitol.

The VEGF-E to be used for therapeutic administration must be sterile. Sterility is readily accomplished by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). The VEGF-E ordinarily will be stored in lyophilized form or as an aqueous solution if it is highly stable to thermal and oxidative denaturation. The pH of the VEGF-E preparations typically will be about from 6 to 8, although higher or lower pH values may also be appropriate in certain instances. It will be understood that use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of salts of the VEGF-E.



If the VEGF-E is to be used parenterally, therapeutic compositions containing the VEGF-E generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

Generally, where the disorder permits, one should formulate and dose the VEGF-E for site-specific delivery. This is convenient in the case of wounds and ulcers.

- 5 Sustained release formulations may also be prepared, and include the formation of microcapsular particles and implantable articles. For preparing sustained-release VEGF-E compositions, the VEGF-E is preferably incorporated into a biodegradable matrix or microcapsule. A suitable material for this purpose is a polylactide, although other polymers of poly-( $\alpha$ -hydroxycarboxylic acids), such as poly-D-(-)-3-hydroxybutyric acid (EP 133,988A), can be used. Other biodegradable polymers include poly(lactones), poly(acetals), poly(orthoesters),  
10 or poly(orthocarbonates). The initial consideration here must be that the carrier itself, or its degradation products, is nontoxic in the target tissue and will not further aggravate the condition. This can be determined by routine screening in animal models of the target disorder or, if such models are unavailable, in normal animals. Numerous scientific publications document such animal models.

- For examples of sustained release compositions, see U.S. Patent No. 3,773,919, EP 58,481A, U.S.  
15 Patent No. 3,887,699, EP 158,277A, Canadian Patent No. 1176565, U. Sidman *et al.*, *Biopolymers* 22, 547 [1983], and R. Langer *et al.*, *Chem. Tech.* 12, 98 [1982].

- When applied topically, the VEGF-E is suitably combined with other ingredients, such as carriers and/or adjuvants. There are no limitations on the nature of such other ingredients, except that they must be pharmaceutically acceptable and efficacious for their intended administration, and cannot degrade the activity  
20 of the active ingredients of the composition. Examples of suitable vehicles include ointments, creams, gels, or suspensions, with or without purified collagen. The compositions also may be impregnated into transdermal patches, plasters, and bandages, preferably in liquid or semi-liquid form.

- For obtaining a gel formulation, the VEGF-E formulated in a liquid composition may be mixed with an effective amount of a water-soluble polysaccharide or synthetic polymer such as polyethylene glycol to form  
25 a gel of the proper viscosity to be applied topically. The polysaccharide that may be used includes, for example, cellulose derivatives such as etherified cellulose derivatives, including alkyl celluloses, hydroxyalkyl celluloses, and alkylhydroxyalkylcelluloses, for example, methylcellulose, hydroxyethyl cellulose, carboxymethyl cellulose, hydroxypropyl methylcellulose, and hydroxypropyl cellulose; starch and fractionated starch; agar; alginic acid and alginates; gum arabic; pullullan; agarose; carrageenan; dextrans; dextrans; fructans; inulin; mannans; xylans;  
30 arabinans; chitosans; glycogens; glucans; and synthetic biopolymers; as well as gums such as xanthan gum; guar gum; locust bean gum; gum arabic; tragacanth gum; and karaya gum; and derivatives and mixtures thereof. The preferred gelling agent herein is one that is inert to biological systems, nontoxic, simple to prepare, and not too runny or viscous, and will not destabilize the VEGF-E held within it.

- Preferably the polysaccharide is an etherified cellulose derivative, more preferably one that is well  
35 defined, purified, and listed in USP, e.g., methylcellulose and the hydroxyalkyl cellulose derivatives, such as hydroxypropyl cellulose, hydroxyethyl cellulose, and hydroxypropyl methylcellulose. Most preferred herein

is methylcellulose.

The polyethylene glycol useful for gelling is typically a mixture of low and high molecular weight polyethylene glycols to obtain the proper viscosity. For example, a mixture of a polyethylene glycol of molecular weight 400-600 with one of molecular weight 1500 would be effective for this purpose when mixed in the proper ratio to obtain a paste.

5       The term "water soluble" as applied to the polysaccharides and polyethylene glycols is meant to include colloidal solutions and dispersions. In general, the solubility of the cellulose derivatives is determined by the degree of substitution of ether groups, and the stabilizing derivatives useful herein should have a sufficient quantity of such ether groups per anhydroglucose unit in the cellulose chain to render the derivatives water soluble. A degree of ether substitution of at least 0.35 ether groups per anhydroglucose unit is generally  
10       sufficient. Additionally, the cellulose derivatives may be in the form of alkali metal salts, for example, the Li, Na, K, or Cs salts.

If methylcellulose is employed in the gel, preferably it comprises about 2-5%, more preferably about 3%, of the gel and the VEGF is present in an amount of about 300-1000 mg per ml of gel.

The dosage to be employed is dependent upon the factors described above. As a general proposition,  
15       the VEGF-E is formulated and delivered to the target site or tissue at a dosage capable of establishing in the tissue a VEGF-E level greater than about 0.1 ng/cc up to a maximum dose that is efficacious but not unduly toxic. This intra-tissue concentration should be maintained if possible by continuous infusion, sustained release, topical application, or injection at empirically determined frequencies.

It is within the scope hereof to combine the VEGF-E therapy with other novel or conventional therapies  
20       (e.g., growth factors such as VEGF, aFGF, bFGF, PDGF, IGF, NGF, anabolic steroids, EGF or TGF- $\alpha$ ) for enhancing the activity of any of the growth factors, including VEGF-E, in promoting cell proliferation, survival, differentiation and repair. It is not necessary that such other treatment drugs be included ~~per se~~ in the compositions of this invention, although this will be convenient where such drugs are proteinaceous. Such admixtures are suitably administered in the same manner and for the same purposes as the VEGF-E used alone. The useful  
25       molar ratio of VEGF-E to such secondary growth factors is typically 1:0.1-10, with about equimolar amounts being preferred.

The compounds of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO polypeptide hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Suitable carrier vehicles and their formulation, inclusive of other  
30       human proteins, e.g., human serum albumin, are described, for example, in *Remington's Pharmaceutical Sciences*, 16th ed., 1980, Mack Publishing Co., edited by Oslo *et al.* the disclosure of which is hereby incorporated by reference. The VEGF-E herein may be administered parenterally to subjects suffering from cardiovascular diseases or conditions, or by other methods that ensure its delivery to the bloodstream in an effective form.

35       Compositions particularly well suited for the clinical administration of VEGF-E hereof employed in the practice of the present invention include, for example, sterile aqueous solutions, or sterile hydratable powders

such as lyophilized protein. It is generally desirable to include further in the formulation an appropriate amount of a pharmaceutically acceptable salt, generally in an amount sufficient to render the formulation isotonic. A pH regulator such as arginine base, and phosphoric acid, are also typically included in sufficient quantities to maintain an appropriate pH, generally from 5.5 to 7.5. Moreover, for improvement of shelf-life or stability of aqueous formulations, it may also be desirable to include further agents such as glycerol. In this manner, variant  
5 t-PA formulations are rendered appropriate for parenteral administration, and, in particular, intravenous administration.

Dosages and desired drug concentrations of pharmaceutical compositions of the present invention may vary depending on the particular use envisioned. For example, in the treatment of deep vein thrombosis or peripheral vascular disease, "bolus" doses, will typically be preferred with subsequent administrations being  
10 given to maintain an approximately constant blood level, preferably on the order of about 3  $\mu\text{g/ml}$ .

However, for use in connection with emergency medical care facilities where infusion capability is generally not available and due to the generally critical nature of the underlying disease (e.g., embolism, infarct), it will generally be desirable to provide somewhat larger initial doses, such as an intravenous bolus.

For the various therapeutic indications referred to for the compounds hereof, the VEGF-E molecules  
15 will be formulated and dosed in a fashion consistent with good medical practice taking into account the specific disorder to be treated, the condition of the individual patient, the site of delivery, the method of administration and other factors known to practitioners in the respective art. Thus, for purposes herein, the "therapeutically effective amount" of the VEGF-E molecules hereof is an amount that is effective either to prevent, lessen the worsening of, alleviate, or cure the treated condition, in particular that amount which is sufficient to enhance  
20 the survival, proliferation or differentiation of targeted cells in vivo. In general a dosage is employed capable of establishing in the tissue that is the target for the therapeutic indication being treated a level of a VEGF-E hereof greater than about 0.1 ng/cm<sup>2</sup> up to a maximum dose that is efficacious but not unduly toxic. It is contemplated that intra-tissue administration may be the choice for certain of the therapeutic indications for the compounds hereof.

25 The human Toll proteins of the present invention can also be used in assays to identify other proteins or molecules involved in Toll-mediated signal transduction. For example, PRO285 and PRO286 are useful in identifying the as of yet unknown natural ligands of human Tolls, or other factors that participate (directly or indirectly) in the activation of and/or signaling through a human Toll receptor, such as potential Toll receptor associated kinases. In addition, inhibitors of the receptor/ligand binding interaction can be identified. Proteins  
30 involved in such binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction. Screening assays can be designed to find lead compounds that mimic the biological activity of a native Toll polypeptide or a ligand for a native Toll polypeptide. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates. Small molecules contemplated include synthetic organic  
35 or inorganic compounds. The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays and cell based assays, which are well characterized in the

art.

*In vitro* assays employ a mixture of components including a Toll receptor polypeptide, which may be part of fusion product with another peptide or polypeptide, e.g., a tag for detecting or anchoring, etc. The assay mixtures may further comprise (for binding assays) a natural intra- or extracellular Toll binding target (i.e. a Toll ligand, or another molecule known to activate and/or signal through the Toll receptor). While native binding targets may be used, it is frequently preferred to use portion of such native binding targets (e.g. peptides), so long as the portion provides binding affinity and avidity to the subject Toll protein conveniently measurable in the assay. The assay mixture also contains a candidate pharmacological agent. Candidate agents encompass numerous chemical classes, through typically they are organic compounds, preferably small organic compounds, and are obtained from a wide variety of sources, including libraries of synthetic or natural compounds. A variety of other reagents may also be included in the mixture, such as, salts, buffers, neutral proteins, e.g. albumin, detergents, protease inhibitors, nuclease inhibitors, antimicrobial agents, etc.

In *in vitro* binding assays, the resultant mixture is incubated under conditions whereby, but for the presence of the candidate molecule, the Toll protein specifically binds the cellular binding target, portion or analog, with a reference binding affinity. The mixture components can be added in any order that provides for the requisite bindings and incubations may be performed at any temperature which facilitates optimal binding. Incubation periods are likewise selected for optimal binding but also minimized to facilitate rapid high-throughput screening.

After incubation, the agent-biased binding between the Toll protein and one or more binding targets is detected by any convenient technique. For cell-free binding type assays, a separation step is often used to separate bound from unbound components. Separation may be effected by precipitation (e.g. TCA precipitation, immunoprecipitation, etc.), immobilization (e.g. on a solid substrate), etc., followed by washing by, for example, membrane filtration (e.g. Whatman's F-15 ion exchange paper, Polysulfone's hydrophobic GFC membrane, etc.), gel chromatography (e.g. gel filtration, affinity, etc.). For Toll-dependent transcription assays, binding is detected by a change in the expression of a Toll-dependent reporter.

Detection may be effected in any convenient way. For cell-free binding assays, one of the components usually comprises or is coupled to a label. The label may provide for direct detection as radioactivity, luminescence, optical or electron density, etc., or indirect detection, such as, an epitope tag, an enzyme, etc. A variety of methods may be used to detect the label depending on the nature of the label and other assay components, e.g. through optical or electron density, radiative emissions, nonradiative energy transfers, etc. or indirectly detected with antibody conjugates, etc.

Nucleic acid encoding the Toll polypeptides disclosed herein may also be used in gene therapy. In gene therapy applications, genes are introduced into cells in order to achieve *in vivo* synthesis of a therapeutically effective genetic product, for example for replacement of a defective gene. "Gene therapy" includes both conventional gene therapy where a lasting effect is achieved by a single treatment, and the administration of gene therapeutic agents, which involves the one time or repeated administration of a therapeutically effective DNA or mRNA. Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain

genes *in vivo*. It has already been shown that short antisense oligonucleotides can be imported into cells where they act as inhibitors, despite their low intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecnik *et al.*, Proc. Natl. Acad. Sci. USA **83**, 4143-4146 [1986]). The oligonucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

5        There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells *in vitro*, or *in vivo* in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells *in vitro* include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. The currently preferred *in vivo* gene transfer techniques include transfection with viral  
10 (typically retroviral) vectors and viral coat protein-liposome mediated transfection (Dzau *et al.*, Trends in Biotechnology **11**, 205-210 [1993]). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate  
15 uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu *et al.*, J. Biol. Chem. **262**, 4429-4432 (1987); and Wagner *et al.*, Proc. Natl. Acad. Sci. USA **87**, 3410-3414 (1990). For review of the currently known gene marking and gene therapy protocols see Anderson *et al.*, Science **256**, 808-813 (1992).

20        The various uses listed in connection with the Toll proteins herein, are also available for agonists of the native Toll receptors, which mimic at least one biological function of a native Toll receptor.  
Neurotrimin as well as other members of the IgLON subfamily of the immunoglobulin superfamily have been identified to have effect upon neural patterning, differentiation, maturation and growth. As a result, PRO337 the human neurotrimin homolog polypeptides would be expected to have utility in diseases which are  
25 characterized by neural disfunction. For example, motoneuron disorders such as amyotrophic lateral sclerosis (Lou Gehrig's disease), Bell's palsy, and various conditions involving spinal muscular atrophy, or paralysis. NGF variant formulations of the invention can be used to treat human neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's Syndrome, nerve deafness, and Meniere's disease. Moreover PRO337 polypeptide may also be used as a cognitive  
30 enhancer, to enhance learning particularly in dementia or trauma, such as those associated with the above diseases.

Further, PRO337 may be employed to treat neuropathy, and especially peripheral neuropathy. "Peripheral neuropathy" refers to a disorder affecting the peripheral nervous system, most often manifested as one or a combination of motor, sensory, sensorimotor, or autonomic neural dysfunction. The wide variety of  
35 morphologies exhibited by peripheral neuropathies can each be attributed uniquely to an equally wide number of causes. For example, peripheral neuropathies can be genetically acquired, can result from a systemic disease,

or can be induced by a toxic agent. Examples include but are not limited to diabetic peripheral neuropathy, distal sensorimotor neuropathy, or autonomic neuropathies such as reduced motility of the gastrointestinal tract or atony of the urinary bladder. Examples of neuropathies associated with systemic disease include post-polio syndrome or AIDS-associated neuropathy; examples of hereditary neuropathies include Charcot-Marie-Tooth disease, Refsum's disease, Abetalipoproteinemia, Tangier disease, Krabbe's disease, Metachromatic leukodystrophy, Fabry's disease, and Dejerine-Sottas syndrome; and examples of neuropathies caused by a toxic agent include those caused by treatment with a chemotherapeutic agent such as vincristine, cisplatin, methotrexate, or 3'-azido-3'-deoxythymidine. Correspondingly, neurotrophin antagonists would be expected to have utility in diseases characterized by excessive neuronal activity.

Endothelin is generated from inactive intermediates, the big endothelins, by a unique processing event catalyzed by the zinc metalloprotease, endothelin converting enzyme (ECE). ECE was recently cloned, and its structure was shown to be a single pass transmembrane protein with a short intracellular N-terminal and a long extracellular C-terminal that contains the catalytic domain and numerous N-glycosylation sites. ECEs cleave the endothelin propeptide between Trp73 and Val74 producing the active peptide, ET, which appears to function as a local rather than a circulating hormone (Rubanyi, G.M. & Polokoff, M.A., *Pharmacological Reviews* 46: 325-415 (1994)). Thus ECE activity is a potential site of regulation of endothelin production and a possible target for therapeutic intervention in the endothelin system. By blocking ECE activity, it is possible to stop the production of ET-1 by inhibiting the conversion of the relatively inactive precursor, big ET-1, to the physiologically active form.

ECE-2 is 64% identical to bovine ECE-2 at the amino acid level. ECE-2 is closely related to ECE-1 (63% identical, 80% conserved), neutral endopeptidase 24.11 and the Kell blood group protein. Bovine ECE-2 is a type II membrane-bound metalloproteinase localized in the trans-Golgi network where it acts as an intracellular enzyme converting endogenous big endothelin-1 into active endothelin (Emoto, N. and Yanangisawa, M., *J. Biol. Chem.* 270: 15262-15268 (1995)). The bovine ECE-2 mRNA expression is highest in parts of the brain, cerebral cortex, cerebellum and adrenal medulla. It is expressed at lower levels in myometrium, testes, ovary, and endothelial cells. Bovine ECE-2 and ECE-1 both are more active on ET-1 as a substrate compared to ET-2 or ET-3, Emoto and Yanangisawa, *supra*.

Human ECE-2 is 736 amino acids in length with a 31 residue amino-terminal tail, a 23 residue transmembrane helix and a 682 carboxy-terminal domain. It is 94% identical to bovine ECE-2 and 64% identical to human ECE-1. The predicted transmembrane domain is highly conserved between the human and bovine ECE-2 proteins and between human ECE-1 and human ECE-2, as are the putative N-linked glycosylation sites, Cys residues conserved in the neutral endopeptidase 24.11 and the Kell blood group protein family and the putative zinc binding motif. The sequence suggests, that like other members of the NEP-ECE-Kell family, human ECE-2 encodes a type II transmembrane zinc-binding metalloproteinase, which, by extrapolation from what is known about bovine ECE-2, is an intracellular enzyme located within the secretory pathway which processes endogenously produced big ET-1 while it is still in the secretory vesicles. Emoto and Yanangisawa, *supra*.

The expression pattern of ECE-2 differs from that observed for ECE-1. Northern blot analysis of

mRNA levels indicated low levels of expression of a 3.3 kb transcript in adult brain (highest in the cerebellum, putamen, medulla and temporal lobe, and lower in the cerebral cortex, occipital lobe and frontal lobe), spinal cord, lung and pancreas and higher levels of a 4.5 kb transcript in fetal brain and kidney. The two transcript sizes probably represent the use of alternative polyadenylation sites as has been observed for bovine ECE-2 (Emoto and Yanangisawa, supra) and ECE-1 (Xu et al., Cell 78: 473-485 (1994). PCR on cDNA libraries indicated low levels of expression in fetal brain, fetal kidney, fetal small intestine and adult testis. Fetal liver, fetal lung and adult pancreas were all negative.

The endothelin (ET) family of peptides have potent vascular, cardiac and renal actions which may be of pathophysiological importance in many human disease states. ET-1 is expressed as an inactive 212 amino acid prepropeptide. The prepropeptide is first cleaved at Arg52-Cys53 and Arg92-Ala93 and then the carboxy terminal Lys91 and Arg92 are trimmed from the protein to generate the propeptide big ET-1. ECEs then cleave the propeptide between Trp73 and Val74, producing the active peptide, ET, which appears to function as a local rather than a circulating hormone (Rubanyi and Polokoff, Pharma. R. 46: 325-415 (1994).

Endothelins may play roles in the pathophysiology of a number of disease states including: 1) cardiovascular diseases (vasospasm, hypertension, myocardial ischemia; reperfusion injury and acute myocardial infarction, stroke (cerebral ischemia), congestive heart failure, shock, atherosclerosis, vascular thickening); 2) kidney disease (acute and chronic renal failure, glomerulonephritis, cirrhosis); 3) lung disease (bronchial asthma, pulmonary hypertension); 4) gastrointestinal disorders (gastric ulcer, inflammatory bowel diseases); 5) reproductive disorders (premature labor, dysmenorrhea, preeclampsia) and 6) carcinogenesis. Rubanyi & Polokoff, supra.

Diseases can be evaluated for the impact of ET upon them by examining: 1) increased production of ETs; 2) increased reactivity to ETs; and/or 3) efficacy of an ET receptor antagonist, antibody or ECE inhibitor. Response to the previous criteria suggest that ETs likely play roles in cerebral vasospasm following subarachnoid hemorrhage, hypertension (fulminant/complications), acute renal failure and congestive heart failure. While inhibitors of ET production or activity have not been used in models of coronary vasospasm, acute myocardial infarction, and atherosclerosis, they do have elevated ET levels and increase reactivity to ETs. Shock and pulmonary hypertension also exhibit elevated ET levels (Rubanyi and Polokoff, supra). Inhibition of ECEs in these conditions may be of therapeutic value.

The expression pattern of ECE-2 differs from that observed for ECE-1. ECE-2 was observed at low levels in the adult brain, lung and pancreas and higher levels in fetal brain and kidney by Northern blot analysis (Fig. 8). PCR revealed low levels of expression in additional tissues: fetal lung, fetal small intestine and adult testis. Fetal liver was negative. A similar pattern was reported for bovine ECE-2 (Emoto and Yanangisawa, supra). It is expressed in brain tissues (cerebral cortex, cerebellum and adrenal medulla), myometrium and testis, and in low levels in ovary and very low levels in many other tissues. Bovine ECE-1 (Xu et al, supra) is more widely and more abundantly expressed. It is observed in vascular endothelial cells of most organs and in some parenchymal cells. With the exception for brain, bovine ECE-2 mRNA was present at lower levels than ECE-1. Applicants believe ECE-2 to be a particularly good target for the therapeutic intervention for diseases

such as cerebral vasospasm following subarachnoid hemorrhage and stroke.

## 92. Anti-PRO Polypeptide Antibodies

The present invention further provides anti-PRO polypeptide antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

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### A. Polyclonal Antibodies

The anti-PRO polypeptide antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

20

### B. Monoclonal Antibodies

The anti-PRO polypeptide antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, *Nature*, 256:495 (1975). In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

25

The immunizing agent will typically include the PRO polypeptide of interest or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103].

30

Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

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Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Rockville, Maryland. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, *J. Immunol.*, 133:3001 (1984); Brodeur *et al.*, *Monoclonal Antibody Production Techniques and Applications*, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against the PRO polypeptide of interest. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, *Anal. Biochem.*, 107:220 (1980).

After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, *supra*]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown *in vivo* as ascites in a mammal.

The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U. S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells, or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4,816,567; Morrison *et al.*, *supra*] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent

heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

*In vitro* methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

5

### C. Humanized Antibodies

The anti-PRO polypeptide antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')<sub>2</sub> or other antigen-binding  
10 subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human  
15 residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise  
20 at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones *et al.*, *Nature*, 321: 522-525 (1986); Riechmann *et al.*, *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-  
25 human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers [Jones *et al.*, *Nature*, 321: 522-525 (1986); Riechmann *et al.*, *Nature*, 332:323-327 (1988); Verhoeyen *et al.*, *Science*, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent  
30 No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

Human antibodies can also be produced using various techniques known in the art, including phage  
35 display libraries [Hoogenboom and Winter, *J. Mol. Biol.*, 227:381 (1991); Marks *et al.*, *J. Mol. Biol.*, 222:581 (1991)]. The techniques of Cole *et al.* and Boerner *et al.* are also available for the preparation of human

monoclonal antibodies (Cole *et al.*, *Monoclonal Antibodies and Cancer Therapy*, Alan R. Liss, p. 77 (1985) and Boerner *et al.*, *J. Immunol.*, 147(1):86-95 (1991)).

#### D. Bispecific Antibodies

5 Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO polypeptide, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain 10 pairs, where the two heavy chains have different specificities [Milstein and Cuello, *Nature*, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker *et al.*, *EMBO* 15 *J.*, 10:3655-3659 (1991).

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in 20 at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable cell. For further details of generating bispecific antibodies see, for example, Sares *et al.*, *Methods in Enzymology*, 121:210 (1986).

#### 25 E. Heteroconjugate Antibodies

Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared *in vitro* 30 using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

#### 35 93. Uses for Anti-PRO Polypeptide Antibodies

The anti-PRO polypeptide antibodies of the invention have various utilities. For example, anti-PRO

polypeptide antibodies may be used in diagnostic assays for a PRO polypeptide, e.g., detecting its expression in specific cells, tissues, or serum. Various diagnostic assay techniques known in the art may be used, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogeneous phases [Zola, Monoclonal Antibodies: A Manual of Techniques, CRC Press, Inc. (1987) pp. 147-158]. The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as  $^3\text{H}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$ ,  $^{35}\text{S}$ , or  $^{125}\text{I}$ , a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter *et al.*, *Nature*, **144**:945 (1962); David *et al.*, *Biochemistry*, **13**:1014 (1974); Pain *et al.*, *J. Immunol. Meth.*, **40**:219 (1981); and Nygren, *J. Histochem. and Cytochem.*, **30**:407 (1982).

Anti-PRO polypeptide antibodies also are useful for the affinity purification of PRO polypeptide from recombinant cell culture or natural sources. In this process, the antibodies against the PRO polypeptide are immobilized on a suitable support, such as a Sephadex resin or filter paper, using methods well known in the art. The immobilized antibody then is contacted with a sample containing the PRO polypeptide to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the sample except the PRO polypeptide, which is bound to the immobilized antibody. Finally, the support is washed with another suitable solvent that will release the PRO polypeptide from the antibody.

Anti-Toll receptor (i.e., anti-PRO285 and anti-PRO286 antibodies) may also be useful in blocking the biological activities of the respective Toll receptors. The primary function of the family of Toll receptors is believed to be to act as pathogen pattern recognition receptors sensing the presence of conserved molecular pattern present on microbes. Lipopolysaccharides (LPS, also known as endotoxins), potentially lethal molecules produced by various bacteria, bind to the lipopolysaccharide binding protein (LBP) in the blood. The complex formed then activates a receptor known as CD14. There is no consensus in the art about what happens next. According to a hypothesis, CD14 does not directly instruct macrophages to produce cytokines, cell adhesion proteins and enzymes involved in the production of lower molecular weight proinflammatory mediators, rather enables LPS to activate a second receptor. Alternatively, it has been suggested that LPS may activate certain receptors directly, without help from LBP or CD14. The data disclosed in the present application indicate that the human toll-like receptors are signaling receptors that are activated by LPS in an LBP and CD14 responsive manner. As this mechanism, under pathophysiologic conditions can lead to an often fatal syndrome called septic shock, anti-Toll receptor antibodies (just as other Toll receptor antagonists) might be useful in the treatment of septic shock. It is foreseen that the different Toll receptors might recognize different pathogens, e.g., various strains of Gram-negative or Gram-positive bacteria. Accordingly, in certain situations, combination therapy with a mixture of antibodies specifically binding different Toll receptors, or the use of bispecific anti-Toll antibodies may be desirable.

It is specifically demonstrated that anti-huTLR2 antibodies are believed to be specifically useful in

blocking the induction of this receptor by LPS. As it has been shown that LPS exposure can lead to septic shock (Parrillo, N. Engl. J. Med. 328, 1471-1477 [1993]), anti-huTLR2 antibodies are potentially useful in the treatment of septic shock.

The foregoing therapeutic and diagnostic uses listed in connection with the anti-Toll receptor antibodies are also applicable to other Toll antagonists, i.e., other molecules (proteins, peptides, small organic molecules, etc.) that block Toll receptor activation and/or signal transduction mediated by Toll receptors.

In view of their therapeutic potentials, the Toll proteins (including variants of the native Toll homologues), and their agonists and antagonists (including but not limited to anti-Toll antibodies) are incorporated in compositions suitable for therapeutic use. Therapeutic compositions are prepared for storage by mixing the active ingredient having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th Edition, Osol, A. Ed. 1980) in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are nontoxic to recipients at the dosages and concentrations employed, and include buffers such as phosphate, citrate and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone, amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as Tween, Pluronics or PEG.

The active ingredients may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively), in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, *supra*.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution.

Therapeutic compositions herein generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration, or by sustained release systems.

Suitable examples of sustained release preparations include semipermeable polymer matrices in the form of shaped articles, e.g. films, or microcapsules. Sustained release matrices include polyesters, hydrogels, polylactides (U.S. Patent 3,773,919, EP 58,481), copolymers of L-glutamic acid and gamma ethyl-L-glutamate (U. Sidman *et al.*, Biopolymers 22 (1): 547-556 [1983]), poly (2-hydroxyethyl-methacrylate) (R. Langer, *et al.*, J. Biomed. Mater. Res. 15: 167-277 [1981] and R. Langer, Chem. Tech. 12: 98-105 [1982]), ethylene vinyl acetate (R. Langer *et al.*, *Id.*) or poly-D-(-)-3-hydroxybutyric acid (EP 133,988). Sustained release compositions

also include liposomes. Liposomes containing a molecule within the scope of the present invention are prepared by methods known per se: DE 3,218,121; Epstein *et al.*, Proc. Natl. Acad. Sci. USA 82: 3688-3692 (1985); Hwang *et al.*, Proc. Natl. Acad. Sci. USA 77: 4030-4034 (1980); EP 52322; EP 36676A; EP 88046; EP 143949; EP 142641; Japanese patent application 83-118008; U.S. patents 4,485,045 and 4,544,545; and EP 102,324. Ordinarily the liposomes are of the small (about 200-800 Angstroms) unilamellar type in which the lipid content is greater than about 30 mol. % cholesterol, the selected proportion being adjusted for the optimal NT-4 therapy.

An effective amount of the active ingredient will depend, for example, upon the therapeutic objectives, the route of administration, and the condition of the patient. Accordingly, it will be necessary for the therapist to titer the dosage and modify the route of administration as required to obtain the optimal therapeutic effect. A typical daily dosage might range from about 1 µg/kg to up to 100 mg/kg or more, depending on the factors mentioned above. Typically, the clinician will administer a molecule of the present invention until a dosage is reached that provides the required biological effect. The progress of this therapy is easily monitored by conventional assays.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

#### EXAMPLES

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Rockville, Maryland.

#### EXAMPLE 1: Extracellular Domain Homology Screening to Identify Novel Polypeptides and cDNA Encoding Therefor

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (e.g., Dayhoff, GenBank), and proprietary databases (e.g. LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul and Gish, Methods in Enzymology 266: 460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a Blast score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA; (<http://bozeman.mbt.washington.edu/phrap.docs/phrap.html>)).

Using this extracellular domain homology screen, consensus DNA sequences were assembled relative

to the other identified EST sequences using phrap. In addition, the consensus DNA sequences obtained were often (but not always) extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above.

Based upon the consensus sequences obtained as described above, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward (.f) and reverse (.r) PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe (.p) sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

## 20 EXAMPLE 2: Isolation of cDNA clones by Amylase Screening

### 1. Preparation of oligo dT primed cDNA library

mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, CA (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 bp and the SalI/NotI linked cDNA was cloned into XhoI/NotI cleaved vector. pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an SfiI restriction enzyme site preceding the XhoI/NotI cDNA cloning sites.

### 2. Preparation of random primed cDNA library

A secondary cDNA library was generated in order to preferentially represent the 5' ends of the primary cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a random primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA was sized to 500-1000 bp, linked with blunt to NotI adaptors, cleaved with SfiI, and cloned into SfiI/NotI cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse amylase sequence (the mature sequence without the secretion signal)

followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transfected yeast colonies.

### 3. Transformation and Detection

5 DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37°C for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampicillin and incubated for 16 hours (37°C). Positive colonies were  
10 scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. CsCl-gradient. The purified DNA was then carried on to the yeast protocols below.

The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR  
15 amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further analysis.

The yeast strain used was HD56-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL<sup>+</sup>, SUC<sup>+</sup>, GAL<sup>+</sup>. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in *sec71*, *sec72*, *sec62*, with truncated *sec71* being most preferred. Alternatively, antagonists (including  
20 antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complete removal of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., 20:1425  
25 (1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30°C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 207 (1994). The overnight culture was then diluted to about  $2 \times 10^6$  cells/ml (approx. OD<sub>600</sub>=0.1) into fresh YEPD broth (500 ml) and regrown to  $1 \times 10^7$  cells/ml (approx. OD<sub>600</sub>=0.4-0.5).

30 The cells were then harvested and prepared for transformation by transfer into GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatant discarded, and then resuspended into sterile water, and centrifuged again in 50 ml falcon tubes at 3,500 rpm in a Beckman GS-6KR centrifuge. The supernatant was discarded and the cells were subsequently washed with LiAc/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM Li<sub>2</sub>OOCCH<sub>3</sub>), and resuspended into LiAc/TE (2.5 ml).

35 Transformation took place by mixing the prepared cells (100 µl) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Gaithersburg, MD) and transforming DNA (1 µg, vol. < 10 µl) in



microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600  $\mu$ l, 40% polyethylene glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Li<sub>2</sub>OOCCH<sub>3</sub>, pH 7.5) was added. This mixture was gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500  $\mu$ l, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells were then diluted into TE (1 ml) and aliquots (200  $\mu$ l) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

The selective media used was a synthetic complete dextrose agar lacking uracil (SCD-Ura) prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 208-210 (1994). Transformants were grown at 30°C for 2-3 days.

The detection of colonies secreting amylase was performed by including red starch in the selective growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by Biely et al., Anal. Biochem., 172:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-100 mM final concentration).

The positive colonies were picked and streaked across fresh selective media (onto 150 mm plates) in order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were determined by their ability to break down starch resulting in a clear halo around the positive colony visualized directly.

#### 4. Isolation of DNA by PCR Amplification

When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30  $\mu$ l) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5  $\mu$ l) was used as a template for the PCR reaction in a 25  $\mu$ l volume containing: 0.5  $\mu$ l KlenTaq (Clontech, Palo Alto, CA); 4.0  $\mu$ l 10 mM dNTP's (Perkin Elmer-Cetus); 2.5  $\mu$ l Kentaq buffer (Clontech); 0.25  $\mu$ l forward oligo 1; 0.25  $\mu$ l reverse oligo 2; 12.5  $\mu$ l distilled water. The sequence of the forward oligonucleotide 1 was:

5'-TGTAACGACGGCCAGTTAAATAGACCTGCAATTATTAATCT-3' (SEQ ID NO:324)

The sequence of reverse oligonucleotide 2 was:

5'-CAGGAAACAGCTATGACCACCTGCACACCTGCAAATCCATT-3' (SEQ ID NO:325)

PCR was then performed as follows:

- |    |              |                  |
|----|--------------|------------------|
| a. | Denature     | 92°C, 5 minutes  |
| b. | 3 cycles of: |                  |
|    | Denature     | 92°C, 30 seconds |
|    | Anneal       | 59°C, 30 seconds |

		Extend	72°C, 60 seconds
5	c.	3 cycles of:	
		Denature	92°C, 30 seconds
		Anneal	57°C, 30 seconds
		Extend	72°C, 60 seconds
	d.	25 cycles of:	
		Denature	92°C, 30 seconds
		Anneal	55°C, 30 seconds
		Extend	72°C, 60 seconds
10	e.	Hold	4°C

The underlined regions of the oligonucleotides annealed to the ADH promoter region and the amylase region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present. Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, signal sequence-fused cDNA resulted in considerably longer nucleotide sequences.

Following the PCR, an aliquot of the reaction (5 µl) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., *supra*. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qiagen Inc., Chatsworth, CA).

### EXAMPLE 3: Isolation of cDNA Clones Encoding Human PRO213

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA28735. Based on the DNA28735 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO213.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGGAGCAGCAATATGCCAGCC-3' (SEQ ID NO:3)

reverse PCR primer 5'-TTTTCCTCCTGTCGGGTTGG-3' (SEQ ID NO:4)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA28735 sequence which had the following nucleotide sequence

hybridization probe

5'-GGTGACACTTGCCAGTCAGATGTGGATGAATGCAGTGCTAGGAGGG-3' (SEQ ID NO:5)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO213 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal lung tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO213 [herein designated as UNQ187 (DNA30943-1163)] (SEQ ID NO:1) and the derived protein sequence for PRO213.

- The entire nucleotide sequence of UNQ187 (DNA30943-1163) is shown in Figure 1 (SEQ ID NO:1).
- 5 Clone UNQ187 (DNA30943-1163) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 336-338 and ending at the stop codon at nucleotide positions 1221-1223 (Figure 1). The predicted polypeptide precursor is 295 amino acids long (Figure 2). Clone UNQ187 (DNA30943-1163) has been deposited with ATCC.

- Analysis of the amino acid sequence of the full-length PRO213 polypeptide suggests that a portion of
- 10 it possesses significant homology to the human growth arrest-specific gene 6 protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO213 amino acid sequence and the following Dayhoff sequences, HSMHC3W5A\_6 and B48089.

#### EXAMPLE 4: Isolation of cDNA Clones Encoding Human PRO274

- 15 A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA36469. Based on the DNA36469 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO274. ESTs proprietary to Genentech were employed in the consensus assembly. The ESTs are shown in
- 20 Figures 5-7 and are herein designated DNA17873, DNA36157 and DNA28929, respectively.

Pairs of PCR primers (forward and reverse) were synthesized:

- forward PCR primer 1 (36469.f1) 5'-CTGATCCGGTCTCTGGTGCCCCCTG-3' (SEQ ID NO:11)
- forward PCR primer 2 (36469.f2) 5'-GCTCTGTCACTCACGCTC-3' (SEQ ID NO:12)
- forward PCR primer 3 (36469.f3) 5'-TCATCTCTTCCCTCTCCC-3' (SEQ ID NO:13)
- 25 forward PCR primer 4 (36469.f4) 5'-CCTTCCGCCACGGAGTTC-3' (SEQ ID NO:14)
- reverse PCR primer 1 (36469.r1) 5'-GGCAAAGTCCACTCCGATGATGTC-3' (SEQ ID NO:15)
- reverse PCR primer 2 (36469.r2) 5'-GCCTGCTGTGGTCACAGGTCTCCG-3' (SEQ ID NO:16)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36469 sequence which had the following nucleotide sequence

- 30 hybridization probe (36469.p1)
- 5'-TCGGGGAGCAGGCCTTGAACCGGGGCATTGCTGCTGTCAAGGAGG-3' (SEQ ID NO:17)

- In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO274 gene using the probe oligonucleotide and one of the PCR primers. RNA
- 35 for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

PRO274 [herein designated as UNQ241 (DNA39987-1184)] (SEQ ID NO:1) and the derived protein sequence for PRO274.

The entire nucleotide sequence of UNQ241 (DNA39987-1184) is shown in Figure 3 (SEQ ID NO:6). Clone UNQ241 (DNA39987-1184) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 83-85 and ending at the stop codon at nucleotide positions 1559-1561 (Figure 3). The predicted polypeptide precursor is 492 amino acids long (Figure 4), has an estimated molecular weight of about 54,241 daltons and an estimated pI of about 8.21. Clone UNQ241 (DNA39987-1184) has been deposited with ATCC and is assigned ATCC deposit no. 209786.

Analysis of the amino acid sequence of the full-length PRO274 polypeptide suggests that it possesses significant homology to the Fn54 protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO274 amino acid sequence and the following Dayhoff sequences, MMFN54S2\_1, MMFN54S1\_1, CELF48C1\_8, CEF38B7\_6, PRP3\_RAT, INL3\_PIG, MTCY07A7\_13, YNAX\_KLEAE, A47234 and HME2\_MOUSE.

#### EXAMPLE 5: Isolation of cDNA Clones Encoding Human PRO300

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA35930. Based on the DNA35930 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO300.

Forward and reverse PCR primers were synthesized:

forward PCR primer 1 (35930.f1) 5'-GCCGCCTCATCTTCACGTTCTTCC-3' (SEQ ID NO:20)

forward PCR primer 2 (35930.f2) 5'-TCATCCAGCTGGTGTCTGCTC-3' (SEQ ID NO:21)

forward PCR primer 3 (35930.f3) 5'-CTTCTTCCACTTCTGCCTGG-3' (SEQ ID NO:22)

forward PCR primer 4 (35930.f4) 5'-CCTGGGCAAAAATGCAAC-3' (SEQ ID NO:23)

reverse PCR primer 1 (35930.r1) 5'-CAGGAATGTAGAAGGCACCCACGG-3' (SEQ ID NO:24)

reverse PCR primer 2 (35930.r2) 5'-TGGCACAGATCTTCACCCACACGG-3' (SEQ ID NO:25)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35930 sequence which had the following nucleotide sequence

hybridization probe (35930.p1)

5'-TGTCCATCATTATGCTGAGCCCGGGCGTGGAGAGTCAGCTCTACAAGCTG-3' (SEQ ID NO:26)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO300 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO300 [herein designated as UNQ263 (DNA40625-1189)] (SEQ ID NO:18) and the derived protein sequence

for PRO300.

The entire nucleotide sequence of UNQ263 (DNA40625-1189) is shown in Figure 8 (SEQ ID NO:18). Clone UNQ263 (DNA40625-1189) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 45-47 and ending at the stop codon at nucleotide positions 1416-1418 (Figure 8). The predicted polypeptide precursor is 457 amino acids long (Figure 9). Clone UNQ263 (DNA40625-1189) has been deposited with ATCC and is assigned ATCC deposit no. 209788.

Analysis of the amino acid sequence of the full-length PRO300 polypeptide suggests that portions of it possess significant homology to the Diff 33 protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO300 amino acid sequence and the following Dayhoff sequence, HSU49188\_1.

10

EXAMPLE 6: Isolation of cDNA Clones Encoding Human PRO284

Two cDNA sequences were isolated in the amylase screen described in Example 2 and those cDNA sequences are herein designated DNA12982 (see Figure 12; human placenta-derived) and DNA15886 (see Figure 13; human salivary gland-derived). The DNA12982 and DNA15886 sequences were then clustered and aligned, giving rise to a consensus nucleotide sequence herein designated DNA18832.

Based on the DNA18832 consensus sequence, oligonucleotide probes were generated and used to screen a human placenta library (LIB89) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

20 PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 (18832.est.f) 5'-TCGTACAGTTACGCTCTCCC-3' (SEQ ID NO:31)

forward PCR primer 2 (18832.f) 5'-CTTGAGGAGCOTCAGAAGCG-3' (SEQ ID NO:32)

reverse PCR primer (18832.r) 5'-ATAACGAATGAAGCCTCGTG-3' (SEQ ID NO:33)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA18832 sequence which had the following nucleotide sequence

hybridization probe (18832.p)

5'-GCTAATATCTGTAAGACGGCAGCTACAGCAGGCATCATTG-3' (SEQ ID NO:34)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO284 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 167-169 and ending at the stop codon found at nucleotide positions 1022-1024 (Figure 10; SEQ ID NO:27). The predicted polypeptide precursor is 285 amino acids long, has a calculated molecular weight of approximately 32,190 daltons and an estimated pI of approximately 9.03. Analysis of the full-length PRO284 sequence shown in Figure 11 (SEQ ID NO:28) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, transmembrane domains from

about amino acid 76 to about amino acid 96 and from about amino acid 171 to about amino acid 195 and a potential N-glycosylation site from about amino acid 153 to about amino acid 156. Clone UNQ247 (DNA23318-1211) has been deposited with ATCC on April 21, 1998 and is assigned ATCC deposit no. 209787.

Analysis of the amino acid sequence of the full-length PRO284 polypeptide suggests that it possesses no significant sequence similarity to any known protein. However, an analysis of the Dayhoff database (version 5 35.45 SwissProt 35) evidenced some degree of homology between the PRO284 amino acid sequence and the following Dayhoff sequences, JQ0124, CELE04A4\_5, AB006451\_1, AF030162\_1, IM23\_YEAST, S71194, NIA\_CUCMA, IM17\_YEAST, I50479 and HUMZFHP\_1.

#### EXAMPLE 7: Isolation of cDNA Clones Encoding Human PRO296

10 A cDNA sequence isolated in the amylase screen as described in Example 2 above was found, by BLAST and FastA sequence alignment, to have sequence homology to a nucleotide sequence encoding sarcoma-associated protein SAS. This cDNA sequence is herein designated DNA23020 (see Figure 16). The DNA23020 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; <http://bozeman.mbt.washington.edu/phrap.docs/phrap.html>). The consensus sequence 20 obtained therefrom is herein designated DNA35858. Two proprietary Genentech ESTs were employed in the assembly wherein those EST sequences are herein identified as DNA21971 (Figure 17; SEQ ID NO:38) and DNA29037 (Figure 18; SEQ ID NO:39).

Based on the DNA35858 consensus sequence, oligonucleotide probes were generated and used to screen a human kidney library (LIB228) library prepared as described in paragraph 1 of Example 2 above. The cloning 25 vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 (35858.f1) 5'-ACCCACGTCTGCGTTGCTGCC-3' (SEQ ID NO:40)

forward PCR primer 2 (35858.f2) 5'-GAGAATATGCTGGAGAGG-3' (SEQ ID NO:41)

30 reverse PCR primer (35858.r1) 5'-AGGAATGCACTAGGATTCGCGCGG-3' (SEQ ID NO:42)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35858 sequence which had the following nucleotide sequence

hybridization probe (35858.p1)

5'-GGCCCCAAAGGCAAGGACAAAGCAGCTGTCAGGGAACCTCCGCCG-3' (SEQ ID NO:43)

35 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

isolate clones encoding the PRO296 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 174-176 and ending at the stop codon found at nucleotide positions 786-788 (Figure 14; SEQ ID NO:35). The predicted polypeptide precursor is 204 amino acids long, has a calculated molecular weight of approximately 22,147 daltons and an estimated pI of approximately 8.37.

5 Analysis of the full-length PRO296 sequence shown in Figure 15 (SEQ ID NO:36) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 34 and transmembrane domains from about amino acid 47 to about amino acid 63, from about amino acid 72 to about amino acid 95 and from about amino acid 162 to about amino acid 182. Clone UNQ260 (DNA39979-1213) has been deposited with ATCC on April 21, 1998 and is assigned ATCC deposit no. 209789.

10 Analysis of the amino acid sequence of the full-length PRO296 polypeptide suggests that it possesses significant sequence similarity to the sarcoma-amplified SAS protein, thereby indicating that PRO296 may be a novel SAS homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO296 amino acid sequence and the following Dayhoff sequences, I58391, GEN11061, SSC2B04\_1, HSU81031\_2, CD63\_RAT, CD63\_MOUSE, CD63\_HUMAN, AF022813\_1,  
15 CD63\_RABIT and CO02\_HUMAN.

#### EXAMPLE 8: Isolation of cDNA Clones Encoding Human PRO329

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA35612. Based on the DNA35612  
20 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO329.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 (35612.f1) 5'-TGGGCTGTGTCCTCATGG-3' (SEQ ID NO:46)

25 forward PCR primer 2 (35612.f2) 5'-TTTCCAGCGCCAATTCTC-3' (SEQ ID NO:47)

reverse PCR primer 1 (35612.r1) 5'-AGTTCTTGGACTGTGATAGCCAC-3' (SEQ ID NO:48)

reverse PCR primer 2 (35612.r2) 5'-AAACTTGGTTGTCCTCAGTGGCTG-3' (SEQ ID NO:49)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35612 sequence which had the following nucleotide sequence

30 hybridization probe (35612.p1)

5'-GTGAGGGACCTGTCTGCACTGAGGAGAGCAGCTGCCACACGGAGG-3' (SEQ ID NO:50)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO329 gene using the probe oligonucleotide and one of the PCR primers. RNA  
35 for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB6).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

PRO329 [herein designated as UNQ291 (DNA40594-1233)] (SEQ ID NO:44) and the derived protein sequence for PRO329.

The entire nucleotide sequence of UNQ291 (DNA40594-1233) is shown in Figure 19 (SEQ ID NO:44). Clone UNQ291 (DNA40594-1233) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon at nucleotide positions 1086-1088 (Figure 19). The predicted polypeptide precursor is 359 amino acids long (Figure 20). The full-length PRO329 protein shown in Figure 20 has an estimated molecular weight of about 38,899 daltons and a pI of about 5.21. Clone UNQ291 (DNA40594-1233) has been deposited with ATCC on February 5, 1998 and is assigned ATCC deposit no. 209617.

Analysis of the amino acid sequence of the full-length PRO329 polypeptide suggests that it possesses significant sequence similarity to a high affinity immunoglobulin F<sub>c</sub> receptor protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO329 amino acid sequence and the following Dayhoff sequences, FCG1\_HUMAN, FCG0\_HUMAN, P\_R91439, P\_R22549, P\_R91438, P\_W00859, P\_R20811, P\_R22550, HUMCD6406\_1 and FCG1\_MOUSE.

#### EXAMPLE 9: Isolation of cDNA Clones Encoding Human PRO362

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42257. Based on the DNA42257 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO362.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 (42257.f1) 5'-TATCCCTCCAATGAGCACCCCTGG-3' (SEQ ID NO:53)

forward PCR primer 2 (42257.f2) 5'-GTCGGAAGACATCCCAACAAG-3' (SEQ ID NO:54)

reverse PCR primer 1 (42257.r1) 5'-CTTCACAATGTCGCTGTGCTGCTC-3' (SEQ ID NO:55)

reverse PCR primer 2 (42257.r2) 5'-AGCCAAATCCAGCAGCTGGCTTAC-3' (SEQ ID NO:56)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42257 sequence which had the following nucleotide sequence

hybridization probe (42257.p1)

5'-TGGATGACCGGAGCCACTACACGTGTGAAGTCACCTGGCAGACTCCTGAT-3' (SEQ ID NO:57)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO362 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue (LIB153).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO362 [herein designated as UNQ317 (DNA45416-1251)] (SEQ ID NO:51) and the derived protein sequence for PRO362.



The entire nucleotide sequence of UNQ317 (DNA45416-1251) is shown in Figure 21 (SEQ ID NO:51). Clone UNQ317 (DNA45416-1251) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 119-121 and ending at the stop codon at nucleotide positions 1082-1084 (Figure 21). The predicted polypeptide precursor is 321 amino acids long (Figure 22). The full-length PRO362 protein shown in Figure 2 has an estimated molecular weight of about 35,544 daltons and a pI of about 8.51. Analysis of the full-length PRO362 polypeptide as shown in Figure 22 evidences the presence of a glycosaminoglycan attachment site at about amino acid 149 to about amino acid 152 and a transmembrane domain from about amino acid 276 to about amino acid 306. Clone UNQ317 (DNA45416-1251) has been deposited with ATCC on February 5, 1998 and is assigned ATCC deposit no. 209620.

Analysis of the amino acid sequence of the full-length PRO362 polypeptide suggests that it possesses significant sequence similarity to the A33 antigen protein and the HCAR protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO362 amino acid sequence and the following Dayhoff sequences, AB002341\_1, HSU55258\_1, HSC7NRCAM\_1, RNU81037\_1, A33\_HUMAN, P\_W14158, NMNCAMRI\_1, HSTITINN2\_1, S71824\_1 and HSU63041\_1.

#### 15 EXAMPLE 10: Isolation of cDNA Clones Encoding Human PRO363

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42828. Based on the DNA42828 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO363.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer (42828.f1) 5'-CCAGTGCACACGAGGCAACGAAGC-3' (SEQ ID NO:60)

reverse PCR primer (42828.r1) 5'-ACTAGGCTGTATGCCTGGGTGGGC-3' (SEQ ID NO:61)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42828 sequence which had the following nucleotide sequence

hybridization probe (42828.p1)

5'-GTATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGC-3' (SEQ ID NO:62)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO363 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO363 [herein designated as UNQ318 (DNA45419-1252)] (SEQ ID NO:58) and the derived protein sequence for PRO363.

The entire nucleotide sequence of UNQ318 (DNA45419-1252) is shown in Figure 23 (SEQ ID NO:58). Clone UNQ318 (DNA45419-1252) contains a single open reading frame with an apparent translational initiation

site at nucleotide positions 190-192 and ending at the stop codon at nucleotide positions 1309-1311 (Figure 23). The predicted polypeptide precursor is 373 amino acids long (Figure 24). The full-length PRO363 protein shown in Figure 24 has an estimated molecular weight of about 41,281 daltons and a pI of about 8.33. A transmembrane domain exists at amino acids 221 to 254 of the amino acid sequence shown in Figure 24 (SEQ ID NO:59). The PRO363 polypeptide also possesses at least two myelin P0 protein domains from about amino acids 15 to 56 and from about amino acids 87 to 116. Clone UNQ318 (DNA45419-1252) has been deposited with ATCC on February 5, 1998 and is assigned ATCC deposit no. 209616.

Analysis of the amino acid sequence of the full-length PRO363 polypeptide suggests that it possesses significant sequence similarity to the cell surface protein HCAR, thereby indicating that PRO363 may be a novel HCAR homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO363 amino acid sequence and the following Dayhoff sequences, HS46KDA\_1, HSU90716\_1, MMCARH\_1, MMCARHOM\_1, MMU90715\_1, A33\_HUMAN, P\_W14146, P\_W14158, A42632 and B42632.

#### EXAMPLE 11: Isolation of cDNA Clones Encoding Human PRO868

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA38133. Based on the DNA38133 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO868.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer (38133.fl) 5'-GTAGCAGTGCACATGGGGTGTGG-3' (SEQ ID NO:65)

reverse PCR primer (38133.rl) 5'-ACCACACATCGTCAGTCTCTGTC-3' (SEQ ID NO:66)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38133 sequence which had the following nucleotide sequence

hybridization probe (38133.p1)

5'-ACGATGATCGCGGGCTCCCTTCTCCTGCTTGGATTCCCTTAGCACCACCAC-3' (SEQ ID NO:67)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO868 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO868 [herein designated as UNQ437 (DNA52594-1270)] (SEQ ID NO:63) and the derived protein sequence for PRO868.

The entire nucleotide sequence of UNQ437 (DNA52594-1270) is shown in Figure 25 (SEQ ID NO:63). Clone UNQ437 (DNA52594-1270) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 325-327 and ending at the stop codon at nucleotide positions 2290-2292 (Figure 25).

The predicted polypeptide precursor is 655 amino acids long (Figure 26). The full-length PRO868 protein shown in Figure 26 has an estimated molecular weight of about 71,845 daltons and a pI of about 8.22. Analysis of the full-length PRO868 polypeptide sequence demonstrates the presence of conserved cysteine-containing domains from about amino acid 66 to about amino acid 78 and from about amino acid 123 to about amino acid 134 of the sequence shown in Figure 26 (SEQ ID NO:3), a TNFR death domain from about amino acid 85 to about amino acid 110, a FASA\_mouse death domain block from about amino acid 159 to about amino acid 175 and a transmembrane domain from about amino acid 347 to about amino acid 375. Clone UNQ437 (DNA52594-1270) has been deposited with ATCC on March 17, 1998 and is assigned ATCC deposit no. 209679

Analysis of the amino acid sequence of the full-length PRO868 polypeptide suggests that it possesses significant sequence similarity to the tumor necrosis factor receptor protein, thereby indicating that PRO868 may be a novel member of the tumor necrosis factor receptor family. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO868 amino acid sequence and the following Dayhoff sequences, RNU94330\_1, P\_R99933, P\_R99945, P\_R99950, HSU94332\_1, CD40\_HUMAN, S63368\_1, TNR2\_HUMAN, MVU87844\_1 AND CVU87837\_1.

#### 15 EXAMPLE 12: Isolation of cDNA Clones Encoding Human PRO382

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA30892. Based on the DNA30892 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO382.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGACATCGCCCTTAAGAAGCTGGC-3' (SEQ ID NO:70)

reverse PCR primer 5'-TACACGTCCCTGTGGTTGCAGATC-3' (SEQ ID NO:71)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA30892 sequence which had the following nucleotide sequence

hybridization probe

5'-CGTTCAATGCAGAAATGATCCAGCCTGTGTGCCTGCCCAACTCTGAAGAG-3' (SEQ ID NO:72)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO382 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO382 [herein designated as UNQ323 (DNA45234-1277)] (SEQ ID NO:68) and the derived protein sequence for PRO382.

The entire nucleotide sequence of UNQ323 (DNA45234-1277) is shown in Figure 27 (SEQ ID NO:68). Clone UNQ323 (DNA45234-1277) contains a single open reading frame with an apparent translational initiation

site at nucleotide positions 126-128 and ending at the stop codon at nucleotide positions 1485-1487 (Figure 27). The predicted polypeptide precursor is 453 amino acids long (Figure 28). The full-length PRO382 protein shown in Figure 28 has an estimated molecular weight of about 49,334 daltons and a pI of about 6.32. Analysis of the native PRO382 amino acid sequence shown in Figure 28 (SEQ ID NO:69) indicates the presence of a putative transmembrane domain from about amino acid 240 to about amino acid 284, a putative signal peptide at about amino acid 1 to about amino acid 20, a putative apple domain at about amino acid 386 to about amino acid 419, a putative Kringle domain at about amino acid 394 to about amino acid 406 and a histidine-containing protease active site at about amino acid 253 to about amino acid 258. Clone UNQ323 (DNA45234-1277) has been deposited with ATCC on March 5, 1998 and is assigned ATCC deposit no. 209654.

Analysis of the amino acid sequence of the full-length PRO382 polypeptide suggests that it possess significant homology to serine protease proteins, thereby indicating that PRO382 may be a novel serine protease. Specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO382 amino acid sequence and the following Dayhoff sequences, HSU75329\_1, ENTK\_MOUSE, HEPS\_HUMAN, AF030065\_1, HEPS\_RAT, PLMN\_PIG, P\_R89430, P\_R89435, PLMN\_HORSE, PLMN\_BOVIN and P\_R83959.

#### EXAMPLE 13: Isolation of cDNA Clones Encoding Human PRO545

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA44706. An EST proprietary to Genentech was employed in the consensus assembly and is herein designated DNA13217 (Figure 31; SEQ ID NO:75). Based on the DNA44706 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO545.

Forward and reverse PCR primers were synthesized:

forward PCR primer 1 5'-GTCTCAGCACGTGTTCTGGTCTCAGGG-3' (SEQ ID NO:76)

forward PCR primer 2 5'-CATGAGCATGTGCACGGC-3' (SEQ ID NO:77)

forward PCR primer 3 5'-TACCTGCACGATGGGCAC-3' (SEQ ID NO:78)

forward PCR primer 4 5'-CACTGGGCACCTCCCTTC-3' (SEQ ID NO:79)

reverse PCR primer 1 5'-CTCCAGGCTGGTCTCCAAGTCCTTC-3' (SEQ ID NO:80)

reverse PCR primer 2 5'-TCCCTGTTGGACTCTGCAGCTTCC-3' (SEQ ID NO:81)

reverse PCR primer 3 5'-CTTCGCTGGGAAGAGTTTG-3' (SEQ ID NO:82)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44706 sequence which had the following nucleotide sequence

hybridization probe

5'-GTGCAACCAACAGATACAAACTCTTCCCAGCGAAGAAGCTGAAAAGCGTC-3'

(SEQ ID NO:83)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO545 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human placenta tissue (LIB90).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO545 [herein designated as UNQ346 (DNA49624-1279)] (SEQ ID NO:73) and the derived protein sequence  
5 for PRO545.

The entire nucleotide sequence of UNQ346 (DNA49624-1279) is shown in Figure 29 (SEQ ID NO:73). Clone UNQ346 (DNA49624-1279) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 311-313 and ending at the stop codon at nucleotide positions 2516-2518 (Figure 29). The predicted polypeptide precursor is 735 amino acids long (Figure 30). The full-length PRO545 protein shown  
10 in Figure 30 has an estimated molecular weight of about 80,177 daltons and a pI of about 7.08. Important regions of the PRO545 amino acid sequence include the signal peptide, corresponding to amino acids 1-28, five potential N-glycosylation sites, from about amino acid 111-114, amino acids 146-149, amino acids 348-351, amino acids 449-452, and amino acids 648-651, and a neutral zinc metalloproteinase, zinc-binding region signature sequence, from about amino acids 344-353. Clone UNQ346 (DNA49624-1279) has been deposited  
15 with ATCC and is assigned ATCC deposit no. 209655.

#### EXAMPLE 14: Isolation of cDNA Clones Encoding Human PRO617

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42798. Based on the DNA42798  
20 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO617.

~~A pair of PCR primers (forward and reverse) were synthesized:~~

forward PCR primer 5'-ACGGGCACACTGGATCCCAAATG-3' (SEQ ID NO:86)

reverse PCR primer 5'-GGTAGAGATGTAGAAGGGCAAGCAAGACC-3' (SEQ ID NO:87)

25 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42798 sequence which had the following nucleotide sequence

hybridization probe

5'-GCTCCCTACCCGTGCAGGTTTCTTCATTTGTTCTTTAACCAGTATGCCG-3' (SEQ ID NO:88)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was  
30 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO617 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO617 [herein designated as UNQ353 (DNA48309-1280)] (SEQ ID NO:1) and the derived protein sequence  
35 for PRO617.

The entire nucleotide sequence of UNQ353 (DNA48309-1280) is shown in Figure 32 (SEQ ID NO:84).

Clone UNQ353 (DNA48309-1280) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 723-725 and ending at the stop codon at nucleotide positions 924-926 (Figure 32). The predicted polypeptide precursor is 67 amino acids long (Figure 33). The full-length PRO617 protein shown in Figure 33 has an estimated molecular weight of about 6,981 daltons and a pI of about 7.47. Analysis of the PRO617 amino acid sequence also evidences the existence of a putative signal peptide from about amino acid 15 to about amino acid 27 and a putative protein kinase C phosphorylation site from about amino acid 41 to about amino acid 43. Clone UNQ353 (DNA48309-1280) has been deposited on March 5, 1998 with ATCC and is assigned ATCC deposit no. 209656.

Analysis of the amino acid sequence of the full-length PRO617 polypeptide suggests that it possesses significant homology to the CD24 protein, thereby indicating that PRO617 may be a novel CD24 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO617 amino acid sequence and the following Dayhoff sequences, CD24\_HUMAN, CD24\_MOUSE, S15785, CD24\_RAT, VGE BPG4, MSE5\_HUMAN, HSMHC3W36A\_2, MLU15184\_8, P R85075, SEPL\_HUMAN and MTCY63\_13.

#### 15 EXAMPLE 15: Isolation of cDNA Clones Encoding Human PRO700

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA30837. Based on the DNA30837 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO700.

Forward and reverse PCR primers were synthesized:

forward PCR primer 1 5'-ATGTTCTTCGCGCCCTGGTG-3' (SEQ ID NO:91)

forward PCR primer 2 5'-CCAAGCCAACACACTCTACAG-3' (SEQ ID NO:92)

reverse PCR primer 1 5'-AAGTGGTCGCCTTGTGCAACGTGC-3' (SEQ ID NO:93)

25 reverse PCR primer 2 5'-GGTCAAAGGGGATATATCGCCAC-3' (SEQ ID NO:94)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA30837 sequence which had the following nucleotide sequence

hybridization probe

5'-GCATGGAAGATGCCAAAGTCTATGTGGCTAAAGTGGACTGCACGGCCCA-3'

30 (SEQ ID NO:95)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO700 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

PRO700 [herein designated as UNQ364 (DNA46776-1284)] (SEQ ID NO:89) and the derived protein sequence for PRO700.

The entire nucleotide sequence of UNQ364 (DNA46776-1284) is shown in Figure 34 (SEQ ID NO:89). Clone UNQ364 (DNA46776-1284) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 1329-1331 (Figure 34).

5 The predicted polypeptide precursor is 432 amino acids long (Figure 35). The full-length PRO700 protein shown in Figure 35 has an estimated molecular weight of about 47,629 daltons and a pI of about 5.90. Important regions of the amino acid sequence of PRO700 include the signal peptide, corresponding to amino acids from about 1 to 33, regions homologous to disulfide isomerase, corresponding to amino acids from about 82-99, 210-255, and 345-360, a tyrosine kinase phosphorylation site, corresponding to amino acids from about 143-151, 10 and an endoplasmic reticulum targeting sequence, corresponding to amino acids from about 429-432. Clone UNQ364 (DNA46776-1284) has been deposited with ATCC and is assigned ATCC Deposit No. 209721.

#### EXAMPLE 16: Isolation of cDNA Clones Encoding Human PRO702

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 15 above, wherein the consensus sequence obtained is herein designated DNA36623. Based on the DNA36623 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO702.

A pair of PCR primers (forward and reverse) were synthesized:

20 forward PCR primer (36623.f1) 5'-CGCTGACTATGTTGCCAAGAGTGG-3' (SEQ ID NO:98)

reverse PCR primer (36623.r1) 5'-GATGATGGAGGCTCCATACCTCAG-3' (SEQ ID NO:99)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36623 sequence which had the following nucleotide sequence

hybridization probe (36623.p1)

25 5'-GTGTTTCATTGGCGTGAATGACCTTGAAAGGGAGGGACAGTACATGTTTCAC-3' (SEQ ID NO:100)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO702 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

30 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO702 [herein designated as UNQ366 (DNA50980-1286)] (SEQ ID NO:96) and the derived protein sequence for PRO702.

The entire nucleotide sequence of UNQ366 (DNA50980-1286) is shown in Figure 36 (SEQ ID NO:96). Clone UNQ366 (DNA50980-1286) contains a single open reading frame with an apparent translational initiation 35 site at nucleotide positions 22-24 and ending at the stop codon at nucleotide positions 853-855 (Figure 36). The predicted polypeptide precursor is 277 amino acids long (Figure 37). The full-length PRO702 protein shown

in Figure 37 has an estimated molecular weight of about 30,645 daltons and a pI of about 7.47. Analysis of the full-length native PRO702 amino acid sequence evidences the presence of a putative signal peptide from about amino acid 1 to about amino acid 25, potential N-glycosylation sites from about amino acid 230 to about amino acid 233 and from about amino acid 258 to about amino acid 261 and a C-type lectin domain signature sequence from about amino acid 248 to about amino acid 270. Clone UNQ366 (DNA50980-1286) has been deposited with  
 5 ATCC on March 31, 1998 and is assigned ATCC deposit no. 209717.

Analysis of the amino acid sequence of the full-length PRO702 polypeptide suggests that it possesses significant sequence similarity to the conglutinin protein, thereby indicating that PRO702 may be a novel conglutinin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO702 amino acid sequence and the following Dayhoff sequences,  
 10 S32436, P\_R75642, P\_W18780, P\_W18781, A53330, AC002528\_1, HSPPA2IC0\_1, CA21\_HUMAN, CA14\_HUMAN and A61262.

#### EXAMPLE 17: Isolation of cDNA Clones Encoding Human PRO703

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1  
 15 above, wherein the consensus sequence obtained is herein designated DNA43047. Based on the DNA43047 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO703.

Forward and reverse PCR primers were synthesized:

20 forward PCR primer 1 5'-GAGAGCCATGGGGCTCCACCTG-3' (SEQ ID NO:103)

reverse PCR primer 1 5'-GGAGAATGTGGCCACAAC-3' (SEQ ID NO:104)

reverse PCR primer 2 5'-GGCCCTGGCACAGTGAATCCATAGACG-3' (SEQ ID NO:105)

reverse PCR primer 3 5'-ATCCAATTTCAGCGGACAC-3' (SEQ ID NO:106)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40654  
 25 sequence which had the following nucleotide sequence

hybridization probe

5'-CCAGTGCCAGGATACCTCTCTTCCCCCAGAGCATAACAGACACG-3'

(SEQ ID NO:107)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was  
 30 screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO703 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO703 [herein designated as UNQ367 (DNA50913-1287)] (SEQ ID NO:101) and the derived protein sequence  
 35 for PRO703.

The entire nucleotide sequence of UNQ367 (DNA50913-1287) is shown in Figure 38 (SEQ ID



NO:101). Clone UNQ367 (DNA50913-1287) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 115-117 and ending at the stop codon at nucleotide positions 2305-2307 (Figure 38). The predicted polypeptide precursor is 730 amino acids long (Figure 39). The full-length PRO703 protein shown in Figure 39 has an estimated molecular weight of about 78,644 daltons, and a pI of about: 7.65. Important regions of the PRO703 amino acid sequence include the signal peptide, a cAMP- and cGMP-dependent protein kinase phosphorylation site, a CUB domain protein motif, N-glycosylation sites and a putative AMP-binding domain signature. Clone UNQ367 (DNA50913-1287) has been deposited with ATCC and is assigned ATCC deposit no. 209716.

#### EXAMPLE 18: Isolation of cDNA Clones Encoding Human PRO705

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43437. Based on the DNA43437 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO705.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AAGCGTGACAGCGGGCACGTC-3' (SEQ ID NO:110)

reverse PCR primer 5'-TGCACAGTCTCTGCAGTGCCCAGG-3' (SEQ ID NO:111)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA43437 sequence which had the following nucleotide sequence

hybridization probe (43437.p1)

5'-GAATGCTGGAACGGGCACAGCAAAGCCAGATACTTGCCTG-3' (SEQ ID NO:112)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO705 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO705 [herein designated as UNQ369 (DNA50914-1289)] (SEQ ID NO:108) and the derived protein sequence for PRO705.

The entire nucleotide sequence of UNQ369 (DNA50914-1289) is shown in Figure 40 (SEQ ID NO:108). Clone UNQ369 (DNA50914-1289) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 566-568 and ending at the stop codon at nucleotide positions 2231-2233 (Figure 40). The predicted polypeptide precursor is 555 amino acids long (Figure 41). The full-length PRO705 protein shown in Figure 41 has an estimated molecular weight of about 62,736 daltons and a pI of about 5.36. Analysis of the full-length PRO705 sequence as shown in Figure 41 evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a eukaryotic DNA topoisomerase I active site from about amino acid 418 to about amino acid 436, and various regions that show homology to various glypican

proteins from about amino acid 237 to about amino acid 279, about amino acid 421 to about amino acid 458, about amino acid 53 to about amino acid 74, about amino acid 466 to about amino acid 504, about amino acid 308 to about amino acid 355, about amino acid 104 to about amino acid 156 and about amino acid 379 to about amino acid 410. Clone UNQ369 (DNA50914-1289) has been deposited with ATCC on March 31, 1998 and is assigned ATCC deposit no.209722.

- 5 Analysis of the amino acid sequence of the full-length PRO705 polypeptide suggests that it possesses significant sequence similarity to the K-glypican protein, thereby indicating that PRO705 may be a novel glypican protein family member. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO705 amino acid sequence and the following Dayhoff sequences, GPCK\_MOUSE, GLYP\_CHICK, GLYP\_RAT, GLYP\_HUMAN, GPC2\_RAT, GPC5\_HUMAN,  
10 GPC3\_HUMAN, GPC3\_RAT, P\_R30168 and CEC03H12\_2.

#### EXAMPLE 19: Isolation of cDNA Clones Encoding Human PRO708

- A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA34024. Based on the DNA34024  
15 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO708.

A pair of PCR primers (forward and reverse) were synthesized:

- forward PCR primer 5'-CCCAACCCAACTGTTTACCTCTGG-3' (SEQ ID NO:115)  
20 reverse PCR primer 5'-CTCTCTGAGTGTACATCTGTGTGG-3' (SEQ ID NO:116)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34024

- ~~sequence which had the following nucleotide sequence~~  
hybridization probe  
5'-GCCACCCTACCTCAGAACTGAAGGAGGTTGGNTATTCAACGCATATGGTCGG-3' (SEQ ID  
25 NO:117)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO708 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255).

- 30 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO708 [herein designated as UNQ372 (DNA48296-1292)] (SEQ ID NO:113) and the derived protein sequence for PRO708.

- The entire nucleotide sequence of UNQ372 (DNA48296-1292) is shown in Figures 42A-B (SEQ ID NO:113). Clone UNQ372 (DNA48296-1292) contains a single open reading frame with an apparent translational  
35 initiation site at nucleotide positions 891-893 and ending at the stop codon at nucleotide positions 2436-2438 (Figures 42A-B). The predicted polypeptide precursor is 515 amino acids long (Figure 43). The full-length

PRO708 protein shown in Figure 43 has an estimated molecular weight of about 56,885 daltons and a pI of about 6.49. Analysis of the PRO708 amino acid sequence shown in Figure 43 (SEQ ID NO:114) evidences the existence of a putative signal peptide at about amino acid 1 to about amino acid 37, putative sulfatase signature sequences at about amino acid 120 to about amino acid 132 and about amino acid 168 to about amino acid 177, a putative tyrosine kinase phosphorylation site from about amino acid 163 to about amino acid 169 and potential N-glycosylation sites from about amino acid 157 to about amino acid 160, about amino acid 306 to about amino acid 309 and about amino acid 318 to about amino acid 321. Clone UNQ372 (DNA48296-1292) has been deposited with ATCC on March 11, 1998 and is assigned ATCC deposit no. 209668.

Analysis of the amino acid sequence of the full-length PRO708 polypeptide suggests that it possesses significant homology to the aryl sulfatase proteins, thereby indicating that PRO708 may be a novel aryl sulfatase homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO708 amino acid sequence and the following Dayhoff sequences, ARSB\_HUMAN, CELC54D2\_2, G02857, STS\_HUMAN, I37186, I37187, GEN12648, CELD1014\_7, GA6S\_HUMAN and SPHM\_HUMAN.

#### EXAMPLE 20: Isolation of cDNA Clones Encoding Human PRO320

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA28739. Based on the DNA28739 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO320.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTGAGTGGCCACATGCTCATG-3' (SEQ ID NO:120)

reverse PCR primer 5'-GGCTGCACGTATGGCTATCCATAG-3' (SEQ ID NO:121)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA28739 sequence which had the following nucleotide sequence

hybridization probe

5'-GATAAACTGTCAGTACAGCTGTGAAGACACAGAAGAAGGGCCACAGTGCC-3' (SEQ ID NO:122)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO320 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO320 [herein designated as UNQ281 (DNA32284-1307)] (SEQ ID NO:118) and the derived protein sequence for PRO320.

The entire nucleotide sequence of UNQ281 (DNA32284-1307) is shown in Figure 44 (SEQ ID NO:118). Clone UNQ281 (DNA32284-1307) contains a single open reading frame with an apparent translational

initiation site at nucleotide positions 135-137 and ending at the stop codon at nucleotide positions 1149-1151 (Figure 44). The predicted polypeptide precursor is 338 amino acids long (Figure 45). The full-length PRO320 protein shown in Figure 45 has an estimated molecular weight of about 37,143 daltons and a pI of about 8.92. Important regions of the PRO320 amino acid sequence include the signal peptide, corresponding to amino acids 1-21, an EGF-like domain cysteine pattern signature, corresponding to amino acids 80-91, and three calcium-binding EGF-like domains, corresponding to amino acids 103-124, 230-251 and 185-206, respectively. Clone UNQ281 (DNA32284-1307) has been deposited with ATCC and is assigned ATCC deposit no. 209670.

#### EXAMPLE 21: Isolation of cDNA Clones Encoding Human PRO324

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA34347. Based on the DNA34347 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO324.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 5'-GCAATGAACTGGGAGCTGC-3' (SEQ ID NO:125)

forward PCR primer 2 5'-CTGTGAATAGCATCCTGGG-3' (SEQ ID NO:126)

forward PCR primer 3 5'-CTTTTCAAGCCACTGGAGGG-3' (SEQ ID NO:127)

reverse PCR primer 1 5'-CTGTAGACATCCAAGCTGGTATCC-3' (SEQ ID NO:128)

reverse PCR primer 2 5'-AAGAGTCTGCATCCACCACTC-3' (SEQ ID NO:129)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34347 sequence which had the following nucleotide sequence

hybridization probe

5'-ACCTGACGCTACTATGGGCCGAGTGGCAGGGACGACGCCCAAGAATG-3' (SEQ ID NO:130)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO324 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB6).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO324 [herein designated as UNQ285 (DNA36343-1310)] (SEQ ID NO: 123) and the derived protein sequence for PRO324.

The entire nucleotide sequence of UNQ285 (DNA36343-1310) is shown in Figure 46 (SEQ ID NO:123). Clone UNQ285 (DNA36343-1310) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 144-146 and ending at the stop codon at nucleotide positions 1011-1013 (Figure 46). The predicted polypeptide precursor is 289 amino acids long (Figure 47). The full-length PRO324 protein shown in Figure 47 has an estimated molecular weight of about 32,268 daltons and a pI of about 9.21. Analysis of the PRO324 polypeptide sequence shown in Figure 47 (SEQ ID NO:124) evidence the presence of

the following: a signal peptide from about amino acid 1 to about amino acid 31, a transmembrane domain from about amino acid 136 to about amino acid 157, tyrosine kinase phosphorylation sites from about amino acid 106 or about amino acid 107 to about amino acid 113 and regions that are homologous to short-chain alcohol dehydrogenase regions from about amino acid 80 to about amino acid 90, from about amino acid 131 to about amino acid 168, from about amino acid 1 to about amino acid 13 and from about amino acid 176 to about amino acid 185. Clone UNQ285 (DNA36343-1310) has been deposited with ATCC on March 30, 1998 and is assigned ATCC deposit no. 209718.

Analysis of the amino acid sequence of the full-length PRO324 polypeptide suggests that it possesses significant sequence similarity to oxidoreductases, thereby indicating that PRO324 may be a novel oxidoreductase homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO324 amino acid sequence and the following Dayhoff sequences, B61209, A69965, YQJQ\_BACSU, D69930, S76124, FABG\_ECOLI, C70023, S77280, FABG\_VIBHA and MTV013\_6.

#### EXAMPLE 22: Isolation of cDNA Clones Encoding Human PRO351

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA35950. Based on the DNA35950 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO351.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CCTGTGCTGTGCCTCGAGCCTGAC-3' (SEQ ID NO:133)

reverse PCR primer 5'-GTGGGCAGCAGTTAGCACCGCCTC-3' (SEQ ID NO:134)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35950 sequence which had the following nucleotide sequence

hybridization probe

5'-GGCTGGCATCATCAGCTTTGCATCAAGCTGTGCCAGGAGGACGC-3'  
(SEQ ID NO:135)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO351 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB230).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO351 [herein designated as UNQ308 (DNA40571-1315)] (SEQ ID NO:131) and the derived protein sequence for PRO351.

The entire nucleotide sequence of UNQ308 (DNA40571-1315) is shown in Figure 48 (SEQ ID NO:131). Clone UNQ308 (DNA40571-1315) contains two open reading frames with an apparent translational initiation site at nucleotide positions 189-191 and a second open reading frame beginning at nucleotide 470, with

the two open reading frames ending at the stop codons at nucleotide positions 363-365 and 2009-2011, respectively (Figure 48). The predicted polypeptide precursor is 571 amino acids long (Figure 49). Important regions of the amino acid sequence of PRO351 include the signal peptide, regions having sequence similarity to serine proteases of the trypsin family, two N-glycosylation sites, and three Kringle domains. Clone UNQ308 (DNA40571-1315) has been deposited with ATCC and is assigned ATCC deposit no. 209784.

5

**EXAMPLE 23: Isolation of cDNA Clones Encoding Human PRO352**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA36950. Based on the DNA36950 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO352.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 5'-CTGGCACAGCTCAACCTCATCTGG-3' (SEQ ID NO:138)

forward PCR primer 2 5'-GCTGTCTGTCTGTCTCATTG-3' (SEQ ID NO:139)

15 forward PCR primer 3 5'-GGACACAGTATACTGACCAC-3' (SEQ ID NO:140)

reverse PCR primer 1 5'-TGCGAACCAGGCAGCTGTAAGTGC-3' (SEQ ID NO:141)

reverse PCR primer 2 5'-TGGAAGAAGAGGGTGGTGATGTGG-3' (SEQ ID NO:142)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36950 sequence which had the following nucleotide sequence

20 hybridization probe

5'-CAGCTGACAGACACCAAACAGCTGGTGCACAGTTTCACCGAAGGC-3' (SEQ ID NO:143)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO352 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

25

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO352 [herein designated as UNQ309 (DNA41386-1316)] (SEQ ID NO:136) and the derived protein sequence for PRO352.

The entire nucleotide sequence of UNQ309 (DNA41386-1316) is shown in Figure 50 (SEQ ID NO:136). Clone UNQ309 (DNA41386-1316) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 152-154 and ending at the stop codon at nucleotide positions 1100-1102 (Figure 50). The predicted polypeptide precursor is 316 amino acids long (Figure 51). The full-length PRO352 protein shown in Figure 2 has an estimated pI of about 4.62. Analysis of the full-length PRO352 sequence evidences the presence of a signal peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 251 to about amino acid 270, potential N-glycosylation sites from about amino acid 91 to about amino acid 94, about amino acid 104 to about amino acid 107, about amino acid 189 to about

35

amino acid 192 and about amino acid 215 to about amino acid 218 and a region having homology to immunoglobulins and MHC from about amino acid 217 to about amino acid 234. Clone UNQ309 (DNA41386-1316) has been deposited with ATCC on March 26, 1998 and is assigned ATCC deposit no. 209703.

Analysis of the amino acid sequence of the full-length PRO352 polypeptide suggests that it possesses significant sequence similarity to the butyrophilin protein, thereby indicating that PRO352 is a novel butyrophilin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO352 amino acid sequence and the following Dayhoff sequences, BUTY\_HUMAN, HSB73\_1, GGCD80\_1, I46690, A33\_HUMAN, P\_R67988, CD86\_MOUSE, P\_R71360, B39371 and D50558\_1.

#### 10 EXAMPLE 24: Isolation of cDNA Clones Encoding Human PRO381

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39651. Based on the DNA39651 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO381.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTTTCCTTGCTTCAGCAACATGAGGC-3' (SEQ ID NO:146)

reverse PCR primer 5'-GCCCAGAGCAGGAGGAATGATGAGC-3' (SEQ ID NO:147)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39651 sequence which had the following nucleotide sequence

hybridization probe

5'-GTGGAAACGCGGTCTTGACTCTCTCGTCACTTCCTTGATGGGGCTTGTG-3' (SEQ ID NO:148)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO381 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO381 [herein designated as UNQ322 (DNA44194-1317)] (SEQ ID NO:144) and the derived protein sequence for PRO381.

The entire nucleotide sequence of UNQ322 (DNA44194-1317) is shown in Figure 52 (SEQ ID NO:144). Clone UNQ322 (DNA44194-1317) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 174-176 and ending at the stop codon at nucleotide positions 807-809 (Figure 52). The predicted polypeptide precursor is 211 amino acids long (Figure 53). The full-length PRO381 protein shown in Figure 53 has an estimated molecular weight of about 24,172 daltons and a pI of about 5.99. Analysis of the full-length PRO381 polypeptide shown in Figure 53 (SEQ ID NO:145) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, a potential N-glycosylation

site from about amino acid 176 to about amino acid 179, potential casein kinase II phosphorylation sites from about amino acid 143 to about amino acid 146, from about amino acid 156 to about amino acid 159, from about amino acid 178 to about amino acid 181, and from about amino acid 200 to about amino acid 203, an endoplasmic reticulum targeting sequence from about amino acid 208 to about amino acid 211, FKBP-type peptidyl-prolyl cis-trans isomerase sites from about amino acid 78 to about amino acid 114 and from about amino acid 118 to about amino acid 131, EF-hand calcium binding domains from about amino acid 191 to about amino acid 203, from about amino acid 184 to about amino acid 203 and from about amino acid 140 to about amino acid 159, and an S-100/ICaBP type calcium binding domain from about amino acid 183 to about amino acid 203. Clone UNQ322 (DNA44194-1317) has been deposited with ATCC on April 28, 1998 and is assigned ATCC deposit no. 209808.

- 10 Analysis of the amino acid sequence of the full-length PRO381 polypeptide suggests that it possesses significant sequence similarity to FKBP immunophilin proteins, thereby indicating that PRO381 may be a novel FKBP immunophilin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO381 amino acid sequence and the following Dayhoff sequences, AF040252\_1, I49669, P\_R93551, S71238, CELC05C8\_1, CEU27353\_1, MIP\_TRYCR, 15 CEZC455\_3, FKB4\_HUMAN and I40718.

#### EXAMPLE 25: Isolation of cDNA Clones Encoding Human PRO386

- A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA40674. Two proprietary Genentech 20 EST sequences were employed in the consensus sequence assembly, wherein those EST sequences are herein designated DNA23350 (Figure 56; SEQ ID NO:151) and DNA23536 (Figure 57; SEQ ID NO:152). Based on the DNA40674 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO386.

- 25 A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-ACGGAGCATGGAGGTCCACAGTAC-3' (SEQ ID NO:153)

reverse PCR primer 5'-GCACGTTTCTCAGCATCACCGAC-3' (SEQ ID NO:154)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40674 sequence which had the following nucleotide sequence

- 30 hybridization probe

5'-CGCCTGCCCTGCACCTTCAACTCCTGCTACACAGTGAACCACAAACAGTT-3' (SEQ ID NO:155)

- In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO386 gene using the probe oligonucleotide and one of the PCR primers. RNA 35 for construction of the cDNA libraries was isolated from human fetal brain tissue (LIB153).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for



PRO386 [herein designated as UNQ326 (DNA45415-1318)] (SEQ ID NO:149) and the derived protein sequence for PRO386.

The entire nucleotide sequence of UNQ326 (DNA45415-1318) is shown in Figure 54 (SEQ ID NO:149). Clone UNQ326 (DNA45415-1318) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 146-148 and ending at the stop codon at nucleotide positions 791-793 (Figure 54). The predicted polypeptide precursor is 215 amino acids long (Figure 55). The full-length PRO386 protein shown in Figure 55 has an estimated molecular weight of about 24,326 daltons and a pI of about 6.32. Analysis of the full-length PRO386 sequence shown in Figure 55 (SEQ ID NO:150) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, a transmembrane domain from about amino acid 161 to about amino acid 179, an immunoglobulin-like fold from about amino acid 83 to about amino acid 127 and potential N-glycosylation sites from about amino acid 42 to about amino acid 45, from about amino acid 66 to about amino acid 69 and from about amino acid 74 to about amino acid 77. Clone UNQ326 (DNA45415-1318) has been deposited with ATCC on April 28, 1998 and is assigned ATCC deposit no. 209810.

Analysis of the amino acid sequence of the full-length PRO386 polypeptide suggests that it possesses significant sequence similarity to the sodium channel beta-2 subunit, thereby indicating that PRO386 is a novel homolog thereof. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO386 amino acid sequence and the following Dayhoff sequences, A57843, MYP0\_HUMAN, GEN14531, JC4024, HS46KDA\_1, HSU90716\_1, D86996\_2, MUSIGLVD\_1, DMU42768\_1 and S19247.

#### 20 EXAMPLE 26: Isolation of cDNA Clones Encoding Human PRO540

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39631. Based on the DNA39631 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO540.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CTGGGGCTACACACGGGGTGAGG-3' (SEQ ID NO:158)

reverse PCR primer 5'-GGTGCCGCTGCAGAAAGTAGAGCG-3' (SEQ ID NO:159)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40654 sequence which had the following nucleotide sequence

hybridization probe

5'-GCCCCAAATGAAAACGGGCCCTACTTCCTGGCCCTCCGCGAGATG-3'

(SEQ ID NO:160)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO540 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO540 [herein designated as UNQ341 (DNA44189-1322)] (SEQ ID NO:156) and the derived protein sequence for PRO540.

The entire nucleotide sequence of UNQ341 (DNA44189-1322) is shown in Figure 58 (SEQ ID NO:156). Clone UNQ341 (DNA44189-1322) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 21-23 and ending at the stop codon at nucleotide positions 1257-1259 (Figure 58). The predicted polypeptide precursor is 412 amino acids long (Figure 59). The full-length PRO540 protein shown in Figure 59 has an estimated molecular weight of about 46,658 daltons and a pI of about 6.65. Important regions of the amino acid sequence of PRO540 include the signal peptide, potential N-glycosylation sites, a potential lipid substrate binding site, a sequence typical of lipases and serine proteins, and a beta-transducin family Trp-Asp repeat. Clone UNQ341 (DNA44189-1322) has been deposited with ATCC and is assigned ATCC deposit no. 209699.

#### EXAMPLE 27: Isolation of cDNA Clones Encoding Human PRO615

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42240. Based on the DNA42240 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO615.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-TGGTCTTCGCCTTGATCGTGTCT-3' (SEQ ID NO:163)

forward PCR primer 5'-GTGTACTGAGCGGCGGTTAG-3' (SEQ ID NO:164)

reverse PCR primer 5'-CTGAAGGTGATGGCTGCCCTCAC-3' (SEQ ID NO:165)

reverse PCR primer 5'-CCAGGAGGCTCATGGGAAAGTCC-3' (SEQ ID NO:166)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42240 sequence which had the following nucleotide sequence:

hybridization probe

5'-CCACGAGTCTAAGCAGATGTACTGCGTGTTCACCGCAACGAGGATGCCT-3'

(SEQ ID NO:167)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO615 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO615 [herein designated as UNQ352 (DNA48304-1323)] (SEQ ID NO:161) and the derived protein sequence for PRO615.

The entire nucleotide sequence of UNQ352 (DNA48304-1323) is shown in Figure 60 (SEQ ID NO:161). Clone UNQ352 (DNA48304-1323) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 51-53 and ending at the stop codon at nucleotide positions 723-725 (Figure 60). The predicted polypeptide precursor is 224 amino acids long (Figure 61). The full-length PRO615 protein shown in Figure 61 has an estimated molecular weight of about 24,810 daltons and a pI of about 4.75.

5 Important regions of the amino acid sequence of PRO615 include a type II transmembrane domain, corresponding to about amino acids 24-43, other transmembrane domains, corresponding to about amino acids 74-90, 108-126, and 145-161, respectively, and a potential N-glycosylation site, corresponding to about amino acids 97-100. Clone UNQ352 (DNA48304-1323) has been deposited with ATCC and is assigned ATCC deposit no. 209811.

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EXAMPLE 28: Isolation of cDNA Clones Encoding Human PRO618

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA30900. Based on the DNA30900 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained

15 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO618.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-TAACAGCTGCCCCACTGCTTCCAGG-3' (SEQ ID NO:171)

reverse PCR primer 5'-TAATCCAGCAGTGCAGGCCGGG-3' (SEQ ID NO:172)

20 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA30900 sequence which had the following nucleotide sequence

hybridization probe

5'-ATGGCCTCCACGGTGCTGTGGACCGTGTTCCTGGGCAAGGTGTGGCAGAA-3'

(SEQ ID NO:173)

25 Screening of the above described library gave rise to the partial cDNA clone designated herein DNA35597 (SEQ ID NO:170). Extension of this sequence using repeated cycles of BLAST and phrap gave rise to a nucleotide sequence designated herein as DNA43335. Primers based upon the DNA43335 consensus sequence were then prepared as follows.

forward PCR primer 5'-TGCCTATGCACTGAGGAGGCAGAAG-3' (SEQ ID NO:174)

30 reverse PCR primer 5'-AGGCAGGGACACAGAGTCCATTAC-3' (SEQ ID NO:175)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA43335 sequence which had the following nucleotide sequence

hybridization probe

5'-AGTATGATTTGCCGTGCACCCAGGGCCAGTGGACGATCCAGAACAGGAGG-3'

35 (SEQ ID NO:176)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with one of the PCR-primer pairs identified above. A positive library was then used to isolate full length clones encoding the PRO618 gene using the second probe oligonucleotide and one of the second set of PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO618 [herein designated as UNQ354 (DNA49152-1324)] (SEQ ID NO:168) and the derived protein sequence for PRO618.

The entire nucleotide sequence of UNQ354 (DNA49152-1324) is shown in Figure 62 (SEQ ID NO:168). Clone UNQ354 (DNA49152-1324) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 73-75 and ending at the stop codon at nucleotide positions 2479-2481 (Figure 62). The predicted polypeptide precursor is 802 amino acids long (Figure 63). The full-length PRO618 protein shown in Figure 63 has an estimated molecular weight of about 88,846 daltons and a pI of about 6.41. Important regions of the amino acid sequence of PRO618 include type II transmembrane domain, a sequence typical of a protease, trypsin family, histidine active site, multiple N-glycosylation sites, two sequences typical of a Kringle domain, two regions having sequence similarity to Kallikrein light chain, and a region having sequence similarity to low-density lipoprotein receptor. Clone UNQ354 (DNA49152-1324) has been deposited with ATCC and is assigned ATCC deposit no. 209813.

#### EXAMPLE 29: Isolation of cDNA Clones Encoding Human PRO719

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA44851. Based on the DNA44851 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO719.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GTGAGCATGAGCGAGCCGTCAC-3' (SEQ ID NO:179)

reverse PCR primer 5'-GCTATTACAACGGTTCTTGCGGCAGC-3' (SEQ ID NO:180)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44851 sequence which had the following nucleotide sequence

hybridization probe

5'-TTGACTCTCTGGTGAATCAGGACAAGCCGAGTTTTCCTTCCAG-3' (SEQ ID NO:181)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO719 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human placenta tissue (LIB90).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO719 [herein designated as UNQ387 (DNA49646-1327)] (SEQ ID NO:177) and the derived protein sequence

for PRO719.

The entire nucleotide sequence of UNQ387 (DNA49646-1327) is shown in Figure 65 (SEQ ID NO:177). Clone UNQ387 (DNA49646-1327) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 223-225 and ending at the stop codon at nucleotide positions 1285-1287 (Figure 65). The predicted polypeptide precursor is 354 amino acids long (Figure 66). The full-length PRO719 protein shown in Figure 66 has an estimated molecular weight of about 39,362 daltons and a pI of about 8.35. Analysis of the full length PRO719 sequence evidences the presence of a signal peptide from about amino acid 1 to about amino acid 16 as shown in Figure 66 (SEQ ID NO:178), a lipase-associated serine-containing active site at about amino acid 163 to about amino acid 172, and two potential N-glycosylation sites from about amino acid 80 to about amino acid 83 and about amino acid 136 to about amino acid 139. Clone UNQ387 (DNA49646-1327) has been deposited with ATCC on March 26, 1998 and is assigned ATCC deposit no. 209705.

Analysis of the amino acid sequence of the full-length PRO719 polypeptide suggests that it possesses significant sequence similarity to the lipoprotein lipase H protein, thereby indicating that PRO719 may be a novel lipoprotein lipase homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO719 amino acid sequence and the following Dayhoff sequences, LIPL\_HUMAN, LIPH\_HUMAN, D83548\_1, A24059\_1, P\_R30740, D88666\_1, A43357, A46696, B43357 and A49488.

#### EXAMPLE 30: Isolation of cDNA Clones Encoding Human PRO724

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA35603. Based on the DNA35603 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO724.

Pairs of PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 5'-GGCTGTCACTGTGGAGACAC-3' (SEQ ID NO:184)

forward PCR primer 2 5'-GCAAGGTCATTACAGCTG-3' (SEQ ID NO:185)

reverse PCR primer 1 5'-AGAACATAGGAGCAGTCCCACTC-3' (SEQ ID NO:186)

reverse PCR primer 2 5'-TGCCTGCTGCTGCACAATCTCAG-3' (SEQ ID NO:187)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35603 sequence which had the following nucleotide sequence

hybridization probe

5'-GGCTATTGCTTGCCTTGGGACAGACCCTGTGGCTTAGGCTCTGGC-3' (SEQ ID NO:188)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO724 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB26).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO724 [herein designated as UNQ389 (DNA49631-1328)] (SEQ ID NO:182) and the derived protein sequence for PRO724.

The entire nucleotide sequence of UNQ389 (DNA49631-1328) is shown in Figure 67 (SEQ ID NO:182). Clone UNQ389 (DNA49631-1328) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 546-548 and ending at the stop codon at nucleotide positions 2685-2687 (Figure 67). The predicted polypeptide precursor is 713 amino acids long (Figure 68). The full-length PRO724 protein shown in Figure 68 has an estimated molecular weight of about 76,193 daltons and a pI of about 5.42. Analysis of the full-length PRO724 amino acid sequence shown in Figure 68 (SEQ ID NO:183) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a transmembrane domain from about amino acid 442 to about amino acid 462 and LDL receptor class A domain regions from about amino acid 152 to about amino acid 171, about amino acid 331 to about amino acid 350, about amino acid 374 to about amino acid 393 and about amino acid 411 to about amino acid 430. Clone UNQ389 (DNA49631-1328) has been deposited with ATCC on April 28, 1998 and is assigned ATCC deposit no. 209806

Analysis of the amino acid sequence of the full-length PRO724 polypeptide suggests that it possesses significant sequence similarity to the human LDL receptor protein, thereby indicating that PRO724 may be a novel LDL receptor homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO724 amino acid sequence and the following Dayhoff sequences, P\_R48547, MMAM2R\_1, LRP2\_RAT, P\_R60517, P\_R47861, P\_R05533, A44513\_1, A30363, P\_R74692 and LMLIPOPHO\_1.

#### EXAMPLE 31: Isolation of cDNA Clones Encoding Human PRO772

One cDNA sequence was isolated in the amylase screen described in Example 2, wherein that cDNA sequence is herein designated DNA43509 (see Figure 71). Based on the DNA43509 sequence, oligonucleotide probes were generated and used to screen a human fetal lung library (LIB25) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A pair of PCR primers (forward and reverse) were synthesized based on the DNA43509 sequence:

forward PCR primer 5'-CGTTTTGCAGAACCTACTCAGGCAG-3' (SEQ ID NO:192)

reverse PCR primer 5'-CCTCCACCAACTGTCAATGTTGTGG-3' (SEQ ID NO:193)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA43509 sequence which had the following nucleotide sequence

hybridization probe

5'-AAAGTGCTGCTGCTGGGTCTGCAGACGCGATGGATAACGT-3' (SEQ ID NO:194)

Using the above described primers and library, a full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 131-133 and ending at the stop codon found at nucleotide positions 587-589 (Figure 69; SEQ ID NO:189). The predicted polypeptide

precursor is 152 amino acids long, has a calculated molecular weight of approximately 17,170 daltons and an estimated pI of approximately 9.62. Analysis of the full-length PRO772 sequence shown in Figure 70 (SEQ ID NO:190) evidences the presence of the following: a potential type II transmembrane domain from about amino acid 26 to about amino acid 42, other potential transmembrane domains from about amino acid 44 to about amino acid 65, from about amino acid 81 to about amino acid 101 and from about amino acid 109 to about amino acid 129, leucine zipper pattern sequences from about amino acid 78 to about amino acid 99 and from about amino acid 85 to about amino acid 106. Clone UNQ410 (DNA49645-1347) has been deposited with ATCC on April 28, 1998 and is assigned ATCC deposit no. 209809.

Analysis of the amino acid sequence of the full-length PRO772 polypeptide suggests that it possesses significant sequence similarity to the human A4 protein, thereby indicating that PRO772 may be a novel A4 protein homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO772 amino acid sequence and the following Dayhoff sequences, HSU93305\_1, A4P\_HUMAN, CELB0454\_2, VPU\_JSRV, CELC12D12\_2, OCCM\_AGRT1, LBPHIG1E\_50, YIGK\_ECOLI, S76245 and P\_R50807.

#### 15 EXAMPLE 32: Isolation of cDNA Clones Encoding Human PRO852

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA34364. Based on the DNA34364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO852.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 5'-CGCAGAAGCTACAGATTCTGG-3' (SEQ ID NO:197)

forward PCR primer 2 5'-GGAAATTGGAGGCCAAAGC-3' (SEQ ID NO:198)

forward PCR primer 3 5'-GGATGTAGCCAGCAACTGTG-3' (SEQ ID NO:199)

25 forward PCR primer 4 5'-GCCTTGGCTCGTTCTCTTC-3' (SEQ ID NO:200)

forward PCR primer 5 5'-GGTCCTGTGCCTGGATGG-3' (SEQ ID NO:201)

reverse PCR primer 1 5'-GACAAGACTACCTCCGTTGGTC-3' (SEQ ID NO:202)

reverse PCR primer 2 5'-TGATGCACAGTTCAGCACCTGTTG-3' (SEQ ID NO:203)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34364 sequence which had the following nucleotide sequence

hybridization probe

5'-CGCTCCAAGGGCTTTGACGTCACAGTGAAGTACACACAAGGAAGCTG-3' (SEQ ID NO:204)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO852 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB228).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO852 [herein designated as UNQ418 (DNA45493-1349)] (SEQ ID NO:195) and the derived protein sequence for PRO852.

The entire nucleotide sequence of UNQ418 (DNA45493-1349) is shown in Figure 72 (SEQ ID NO:195). Clone UNQ418 (DNA45493-1349) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 16748-1650 (Figure 72). The predicted polypeptide precursor is 518 amino acids long (Figure 73). The full-length PRO852 protein shown in Figure 73 has an estimated molecular weight of about 56,180 daltons and a pI of about 5.08. Analysis of the full-length PRO852 sequence shown in Figure 73 (SEQ ID NO:196) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, a transmembrane domain from about amino acid 466 to about amino acid 494, potential N-glycosylation sites from about amino acid 170 to about amino acid 173 and about amino acid 366 to about amino acid 369, leucine zipper sequence pattern blocks from about amino acid 10 to about amino acid 31 and from about amino acid 197 to about amino acid 218 and blocks of amino acids having sequence homology to eukaryotic and viral aspartyl proteases from about amino acid 109 to about amino acid 118, from about amino acid 252 to about amino acid 261 and from about amino acid 298 to about amino acid 310. Clone UNQ418 (DNA45493-1349) has been deposited with ATCC on April 28, 1998 and is assigned ATCC deposit no. 209805.

Analysis of the amino acid sequence of the full-length PRO852 polypeptide suggests that it possesses significant sequence similarity to various protease proteins, thereby indicating that PRO852 may be a novel protease protein or homolog thereof. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO852 amino acid sequence and the following Dayhoff sequences, PEPC\_HUMAN, S66516, S66517, PEPE\_CHICK, CATD\_HUMAN, P\_R74207, ~~CARP\_YEAST~~, ~~PEP1\_RABIT~~, ~~CATE\_HUMAN~~ and ~~RENI\_MOUSE~~.

#### EXAMPLE 33: Isolation of cDNA Clones Encoding Human PRO853

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43050. Based on the DNA43050 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO853.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CTTCATGGCCTTGGACTTGGCCAG-3' (SEQ ID NO:207)

reverse PCR primer 5'-ACGCCAGTGGCCTCAAGCTGGTTG-3' (SEQ ID NO:208)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA43050 sequence which had the following nucleotide sequence

hybridization probe

5'-CTTCTGAGCTCTGAGCCACGGTTGGACATCCTCATCCACAATGC-3' (SEQ ID NO:209)



In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO853 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB228).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO853 [herein designated as UNQ419 (DNA48227-1350)] (SEQ ID NO:205) and the derived protein sequence for PRO853.

The entire nucleotide sequence of UNQ419 (DNA48227-1350) is shown in Figure 74 (SEQ ID NO:205). Clone UNQ419 (DNA48227-1350) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 128-130 and ending at the stop codon at nucleotide positions 1259-1261 (Figure 74). The predicted polypeptide precursor is 377 amino acids long (Figure 75). The full-length PRO853 protein shown in Figure 75 has an estimated molecular weight of about 40,849 daltons and a pI of about 7.98. Important regions of the amino acid sequence of PRO853 include the signal peptide, corresponding to amino acids from about 1 to about 16 of SEQ ID NO:206, the glycosaminoglycan attachment site, corresponding to amino acids from about 46 to about 49 of SEQ ID NO:206, and two sequences typical of the short-chain alcohol dehydrogenase family, corresponding to amino acids from about 37 to about 49 and about 114 to about 124 of SEQ ID NO:206, respectively. Clone UNQ419 (DNA48227-1350) has been deposited with ATCC and is assigned ATCC deposit no. 209812.

#### EXAMPLE 34: Isolation of cDNA Clones Encoding Human PRO860

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA38137. Based on the DNA38137 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO860.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-GAAGGGACCTACATGTGTGTGGCC-3' (SEQ ID NO:212)

reverse PCR primer 5'-ACTGACCTTCCAGCTGAGCCACAC-3' (SEQ ID NO:213)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40654 sequence which had the following nucleotide sequence

hybridization probe

5'-AGGACTACACGGAGCCTGTGGAGCTTCTGGCTGTGCGAATTCAGCTGGAA-3'

(SEQ ID NO:214)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO860 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB26).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for

PRO860 [herein designated as UNQ421 (DNA41404-1352)] (SEQ ID NO:210) and the derived protein sequence for PRO860.

The entire nucleotide sequence of UNQ421 (DNA41404-1352) is shown in Figures 76A-B (SEQ ID NO:210). Clone UNQ421 (DNA41404-1352) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 3013-3015 (Figures 76A-B). The predicted polypeptide precursor is 985 amino acids long (Figure 77). The full-length PRO860 protein shown in Figure 77 has an estimated molecular weight of about 105,336 daltons and a pI of about 6.55. Important regions of the amino acid sequence of PRO860 include the transmembrane region corresponding to about amino acids 448-467, the extracellular domain, corresponding to amino acids about 1-447, several N-glycosylation sites, numerous N-myristoylation sites and a sequence typical of phosphotyrosine interaction domain proteins.. Clone UNQ421 (DNA41404-1352) has been deposited with ATCC and is assigned ATCC deposit no. 209844.

#### EXAMPLE 35: Isolation of cDNA Clones Encoding Human PRO846

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39949. Based on the DNA39949 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO846.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CCCTGCAGTGCACCTACAGGGAAG-3' (SEQ ID NO:217)

reverse PCR primer 5'-CTGTCTTCCCCTGCTTGGCTGTGG-3' (SEQ ID NO:218)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39949 sequence which had the following nucleotide sequence

hybridization probe

5'-GGTGCAGGAAGGGTGGGATCCTCTTCTCTCGCTGCTCTGGCCACATC-3'  
(SEQ ID NO:219)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO846 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO846 [herein designated as UNQ422 (DNA44196-1353)] (SEQ ID NO:215) and the derived protein sequence for PRO846.

The entire nucleotide sequence of UNQ422 (DNA44196-1353) is shown in Figure 78 (SEQ ID NO:215). Clone UNQ422 (DNA44196-1353) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon at nucleotide positions 1021-1023

(Figure 78). The predicted polypeptide precursor is 332 amino acids long (Figure 79). The full-length PRO846 protein shown in Figure 79 has an estimated molecular weight of about 36,143 daltons and a pI of about 5.89. Important regions of the amino acid sequence of PRO846 include the signal peptide, the transmembrane domain, an N-glycosylation site, a sequence typical of fibrinogen beta and gamma chains C-terminal domain, and a sequence typical of Ig like V-type domain as shown in Figure 79. Clone UNQ422 (DNA44196-1353) has been deposited with ATCC and is assigned ATCC deposit no. 209847.

#### EXAMPLE 36: Isolation of cDNA Clones Encoding Human PRO862

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA47370. Based on the DNA47370 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO862.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-GGGATCATGTTGTTGGCCCTGGTC-3' (SEQ ID NO:222)

15 reverse PCR primer 5'-GCAAGGCAGACCCAGTCAGCCAG-3' (SEQ ID NO:223)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47370 sequence which had the following nucleotide sequence

hybridization probe

5'-CTGCCTGCTACCCCTCCAAGTGAGGCCAAGCTCTACGGTCGTTGTG-3'

20 (SEQ ID NO:225)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO862 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human pancreas tissue (LIB55).

25 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO862 [herein designated as UNQ424 (DNA52187-1354)] (SEQ ID NO:220) and the derived protein sequence for PRO862.

The entire nucleotide sequence of UNQ424 (DNA52187-1354) is shown in Figure 80 (SEQ ID NO:220). Clone UNQ424 (DNA52187-1354) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 410-412 and ending at the stop codon at nucleotide positions 848-850 (Figure 80). The predicted polypeptide precursor is 146 amino acids long (Figure 81). The full-length PRO862 protein shown in Figure 81 has an estimated molecular weight of about 16,430 daltons and a pI of about 5.05. Important regions of the amino acid sequence of PRO862 include the signal peptide, an N-myristoylation site, and sequences having similarity to region to Alpha-lactalbumin/lysozyme C proteins as shown in Figure 81.

35 Clone UNQ424 (DNA52187-1354) has been deposited with the ATCC and is assigned ATCC deposit no. 209845.

**EXAMPLE 37: Isolation of cDNA Clones Encoding Human PRO864**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA40666. Based on the DNA40666 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO864.

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-GCTGCAGCTGCAAATTCCTGG-3' (SEQ ID NO:227)

reverse PCR primer 5'-TGGTGGGAGACTGTTTAAATTATCGGCC-3' (SEQ ID NO:228)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40666 sequence which had the following nucleotide sequence

hybridization probe

5'-TGCTTCGTCAAGTGCCGGCAGTGCCAGCGGCTCGTGGAGTT-3'

(SEQ ID NO:229)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO864 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue (LIB153).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO864 [herein designated as UNQ426 (DNA48328-1355)] (SEQ ID NO:225) and the derived protein sequence for PRO864.

The entire nucleotide sequence of UNQ426 (DNA48328-1355) is shown in Figure 82 (SEQ ID NO:225). Clone UNQ426 (DNA48328-1355) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 37-39 and ending at the stop codon at nucleotide positions 1090-1092 (Figure 82). The predicted polypeptide precursor is 351 amino acids long (Figure 83). The full-length PRO864 protein shown in Figure 83 has an estimated molecular weight of about 39,052 and a pI of about 8.97. Important regions of the amino acid sequence of PRO864 include the signal peptide, two N-glycosylation sites, a Wnt-1 family signature sequence, and sequence regions homologous to Wnt-1 family proteins as shown in Figure 83. Clone UNQ426 (DNA48328-1355) has been deposited with ATCC and is assigned ATCC deposit no. 209843.

**EXAMPLE 38: Isolation of cDNA Clones Encoding Human PRO792**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA38106. Based on the DNA38106 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO792.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCGAGAACTGTGTCATGATGCTGC-3' (SEQ ID NO:232)

reverse PCR primer 5'-GTTTCTGAGACTCAGCAGCGGTGG-3' (SEQ ID NO:233)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38106 sequence which had the following nucleotide sequence

hybridization probe

5 5'-CACCGTGTGACAGCGAGAAGGACGGCTGGATCTGTGAGAAAAGGCACAAC-3' (SEQ ID NO:234)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO792 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255).

10 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO792 [herein designated as UNQ431 (DNA56352-1358)] (SEQ ID NO:230) and the derived protein sequence for PRO792.

The entire nucleotide sequence of UNQ431 (DNA56352-1358) is shown in Figure 84 (SEQ ID NO:230). Clone UNQ431 (DNA56352-1358) contains a single open reading frame with an apparent translational  
15 initiation site at nucleotide positions 67-69 and ending at the stop codon at nucleotide positions 946-948 (Figure 84). The predicted polypeptide precursor is 293 amino acids long (Figure 85). The full-length PRO792 protein shown in Figure 85 has an estimated molecular weight of about 32,562 daltons and a pI of about 6.53. Analysis of the full-length PRO792 sequence shown in Figure 85 (SEQ ID NO:231) evidences the presence of the following: a type II transmembrane domain from about amino acid 31 to about amino acid 54, potential N-  
20 glycosylation sites from about amino acid 73 to about amino acid 76 and from about amino acid 159 to about amino acid 162, a leucine zipper amino acid sequence pattern from about amino acid 102 to about amino acid 123, potential N-myristoylation sites from about amino acid 18 to about amino acid 23, from about amino acid 133 to about amino acid 138 and from about amino acid 242 to about amino acid 247 and a C-type lectin domain signature block from about amino acid 264 to about amino acid 287. Clone UNQ431 (DNA56352-1358) has been  
25 deposited with ATCC on May 6, 1998 and is assigned ATCC deposit no. 209846.

Analysis of the amino acid sequence of the full-length PRO792 polypeptide suggests that it possesses significant sequence similarity to the CD23 protein, thereby indicating that PRO792 may be a novel CD23 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO792 amino acid sequence and the following Dayhoff sequences, S34198,  
30 A07100\_1, A05303\_1, P\_R41689, P\_P82839, A10871\_1, P\_R12796, P\_R47199, A46274 and P\_R32188.

#### EXAMPLE 39: Isolation of cDNA Clones Encoding Human PRO866

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA44708. Based on the DNA44708  
35 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for

PRO866.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 5'-CAGCACTGCCAGGGGAAGAGGG-3' (SEQ ID NO:237)

forward PCR primer 2 5'-CAGGACTCGCTACGTCCG-3' (SEQ ID NO:238)

forward PCR primer 3 5'-CAGCCCCTTCTCCTCCTTTCTCCC-3' (SEQ ID NO:239)

5 reverse PCR primer 1 5'-GCAGTTATCAGGGACGCACTCAGCC-3' (SEQ ID NO:240)

reverse PCR primer 2 5'-CCAGCGAGAGGCAGATAG-3' (SEQ ID NO:241)

reverse PCR primer 3 5'-CGGTCACCGTGTCTGCGGGATG-3' (SEQ ID NO:242)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44708 sequence which had the following nucleotide sequence

10 hybridization probe

5'-CAGCCCCTTCTCCTCCTTTCTCCACGTCCTATCTGCCTCTC-3' (SEQ ID NO:243)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO866 gene using the probe oligonucleotide and one of the PCR primers.

15 RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB228).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO866 [herein designated as UNQ435 (DNA53971-1359)] (SEQ ID NO:235) and the derived protein sequence for PRO866.

The entire nucleotide sequence of UNQ435 (DNA53971-1359) is shown in Figure 86 (SEQ ID NO:235). Clone UNQ435 (DNA53971-1359) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 275-277 and ending at the stop codon at nucleotide positions 1268-1270 (Figure 86). The predicted polypeptide precursor is 331 amino acids long (Figure 87). The full-length PRO866 protein shown in Figure 87 has an estimated molecular weight of about 35,844 daltons and a pI of about 5.45. Analysis of the full-length PRO866 sequence shown in Figure 87 (SEQ ID NO:236) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26. Clone UNQ435 (DNA53971-1359) has been deposited with ATCC on April 7, 1998 and is assigned ATCC deposit no. 209750.

Analysis of the amino acid sequence of the full-length PRO866 polypeptide suggests that it possesses significant sequence similarity to the mindin/spondin family of proteins, thereby indicating that PRO866 may be a novel mindin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO866 amino acid sequence and the following Dayhoff sequences, AB006085\_1, AB006084\_1, AB006086\_1, AF017267\_1, CWU42213\_1, AC004160\_1, CPMICRP\_1, S49108, A48569 and I46687.

#### EXAMPLE 40: Isolation of cDNA Clones Encoding Human PRO871

35 A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA40324. Based on the DNA40324

consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO871.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 5'-TGCGGAGATCCTACTGGCACAGGG-3' (SEQ ID NO:246)

5 forward PCR primer 2 5'-CGAGTTAGTCAGAGCATG-3' (SEQ ID NO:247)

forward PCR primer 3 5'-CAGATGGTGCTGTTGCCG-3' (SEQ ID NO:248)

reverse PCR primer 1 5'-CAACTGGAACAGGAACTGAGATGTGGATC-3' (SEQ ID NO:249)

reverse PCR primer 2 5'-CTGGTTCAGCAGTGCAAGGGTCTG-3' (SEQ ID NO:250)

reverse PCR primer 3 5'-CCTCTCCGATTAAAACGC-3' (SEQ ID NO:251)

10 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40324 sequence which had the following nucleotide sequence

hybridization probe

5'-GAGAGGACTGGTTGCCATGGCAAATGCTGGTTCTCATGATAATGG-3' (SEQ ID NO:252)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was  
15 screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO871 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO871 [herein designated as UNQ438 (DNA50919-1361)] (SEQ ID NO:244) and the derived protein sequence  
20 for PRO871.

The entire nucleotide sequence of UNQ438 (DNA50919-1361) is shown in Figure 88 (SEQ ID NO:244). Clone UNQ438 (DNA50919-1361) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 191-193 and ending at the stop codon at nucleotide positions 1607-1609 (Figure 88). The predicted polypeptide precursor is 472 amino acids long (Figure 89). The full-length PRO871  
25 protein shown in Figure 89 has an estimated molecular weight of about 53,847 daltons and a pI of about 5.75. Analysis of the full-length PRO871 sequence shown in Figure 89 (SEQ ID NO:245) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 109 to about amino acid 112 and from about amino acid 201 to about amino acid 204, a cyclophilin-type peptidyl-prolyl cis-trans isomerase signature sequence from about amino acid 49 to about amino  
30 acid 66 and regions that are homologous to cyclophilin-type peptidyl-prolyl cis-trans isomerases from about amino acid 96 to about amino acid 140, from about amino acid 49 to about amino acid 89 and from about amino acid 22 to about amino acid 51. Clone UNQ438 (DNA50919-1361) has been deposited with ATCC on May 6, 1998 and is assigned ATCC deposit no. 209848.

Analysis of the amino acid sequence of the full-length PRO871 polypeptide suggests that it possesses  
35 significant sequence similarity to the cyclophilin family of proteins, thereby indicating that PRO871 may be a novel cyclophilin protein family member. More specifically, an analysis of the Dayhoff database (version 35.45

SwissProt 35) evidenced significant homology between the PRO871 amino acid sequence and the following Dayhoff sequences, SPBC16H5\_5, S64705, YAL5\_SCHPO, CYP4\_CAEEL, CELC34D4\_7, CYPA\_CAEEL, HUMORF006\_1, CYPI\_MYCTU, AF043642\_1 and HSSRCYP\_1.

**EXAMPLE 41: Isolation of cDNA Clones Encoding Human PRO873**

5 A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39621. Based on the DNA39621 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO873.

10 A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGGTGCCTGCAGGAGTCCTGGGG-3' (SEQ ID NO:255)

reverse PCR primer 5'-CCACCTCAGGAAGCCGAAGATGCC-3' (SEQ ID NO:256)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39621 sequence which had the following nucleotide sequence:

15 hybridization probe

5'-GAACGGTACAAGTGGCTGCGCTTCAGCGAGGACTGTCTGTACCTG-3' (SEQ ID NO:257)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO873 gene using the probe oligonucleotide and one of the PCR primers. RNA  
20 for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO873 [herein designated as UNQ440 (DNA44179-1362)] (SEQ ID NO:253) and the derived protein sequence for PRO873.

The entire nucleotide sequence of UNQ440 (DNA44179-1362) is shown in Figure 90 (SEQ ID  
25 NO:253). Clone UNQ440 (DNA44179-1362) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 139-141 and ending at the stop codon at nucleotide positions 1774-1776 (Figure 90). The predicted polypeptide precursor is 545 amino acids long (Figure 91). The full-length PRO873 protein shown in Figure 91 has an estimated molecular weight of about 58,934 daltons and a pI of about 9.45. Analysis of the full-length PRO873 sequence shown in Figure 91 (SEQ ID NO:254) evidences the presence of  
30 the following features: a signal peptide from about amino acid 1 to about amino acid 29; a carboxylesterase type-B serine active site at about amino acid 312 to about amino acid 327; a carboxylesterase type-B signature 2 motif at about amino acid 218 to about amino acid 228; and three potential N-glycosylation sites at about amino acid 318 to about amino acid 321, about amino acid 380 to about amino acid 383, and about amino acid 465 to about amino acid 468. Clone UNQ440 (DNA44179-1362) has been deposited with ATCC on May 6, 1998 and is  
35 assigned ATCC deposit no. 209851.

Analysis of the amino acid sequence of the full-length PRO873 polypeptide suggests that it possesses



significant sequence similarity to a human liver carboxylesterase, thereby indicating that PRO873 may be a novel carboxylesterase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO873 amino acid sequence and the following Dayhoff sequences: ES10\_RAT, GEN12405, AB010633\_1, EST4\_RAT, A48809, SASB\_ANAPL, RNU41662\_1, RNU22952\_1, BAL\_RAT, GEN13522.

5

**EXAMPLE 42: Isolation of cDNA Clones Encoding Human PRO940**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA47442. Based on the DNA47442 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained  
10 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO940.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CAAAGCTGCGCCTGGTCTGTG-3' (SEQ ID NO:260)

reverse PCR primer 5'-TTCTGGAGCCCAGAGGGTGCTGAG-3' (SEQ ID NO:262)

15 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47442 sequence which had the following nucleotide sequence

hybridization probe

5'-GGAGCTGCCACCCATTCAAATGGAGCACGAAGGAGAGTTCACCTG-3' (SEQ ID NO:263)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was  
20 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO940 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO940 [herein designated as UNQ477 (DNA54002-1367)] (SEQ ID NO:258) and the derived protein sequence  
25 for PRO940.

The entire nucleotide sequence of UNQ477 (DNA54002-1367) is shown in Figure 92 (SEQ ID NO:258). Clone UNQ477 (DNA54002-1367) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 1678-1680 (Figure 92). The predicted polypeptide precursor is 544 amino acids long (Figure 93). The full-length PRO940  
30 protein shown in Figure 93 has an estimated molecular weight of about 60,268 daltons and a pI of about 9.53. Analysis of the full-length PRO940 sequence shown in Figure 93 (SEQ ID NO:259) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 100 to about amino acid 103, from about amino acid 297 to about amino acid 300 and from about amino acid 306 to about amino acid 309 and an immunoglobulin and major histocompatibility  
35 complex signature sequence block from about amino acid 365 to about amino acid 371. Clone UNQ477 (DNA54002-1367) has been deposited with ATCC on April 7, 1998 and is assigned ATCC deposit no. 209754.

Analysis of the amino acid sequence of the full-length PRO940 polypeptide suggests that it possesses significant sequence similarity to CD33 and the OB binding protein-2. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO940 amino acid sequence and the following Dayhoff sequences, CD33\_HUMAN, HSU71382\_1, HSU71383\_1, D86359\_1, PGBM\_HUMAN, MAGS\_MOUSE, D86983\_1, C22B\_HUMAN, P\_W01002 and HVU24116\_1.

5

**EXAMPLE 43: Isolation of cDNA Clones Encoding Human PRO941**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA35941. An EST sequence proprietary to Genentech was employed in the assembly and is herein designated DNA6415 (Figure 96; SEQ ID NO:265).

10 Based on the DNA35941 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO941.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTTGACTGTCTCTGAATCTGCACCC-3' (SEQ ID NO:266)

15 reverse PCR primer 5'-AAGTGGTGAAGCCTCCAGTGTGG-3' (SEQ ID NO:267)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35941 sequence which had the following nucleotide sequence

hybridization probe

5'-CCACTACGGTATTAGAGCAAAAGTTAAAAACCATCATGGTTCCTGGAGCAGC-3' (SEQ ID NO:268)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO941 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

25 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO941 [herein designated as UNQ478 (DNA53906-1368)] (SEQ ID NO:263) and the derived protein sequence for PRO941.

The entire nucleotide sequence of UNQ478 (DNA53906-1368) is shown in Figure 94 (SEQ ID NO:263). Clone UNQ478 (DNA53906-1368) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 37-39 and ending at the stop codon at nucleotide positions 2353-2355 (Figure 94). The predicted polypeptide precursor is 772 amino acids long (Figure 95). The full-length PRO941 protein shown in Figure 95 has an estimated molecular weight of about 87,002 daltons and a pI of about 4.64. Analysis of the full-length PRO941 sequence shown in Figure 95 (SEQ ID NO:264) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 57 to about amino acid 60, from about amino acid 74 to about amino acid 77, from about amino acid 419 to about amino acid 422, from about amino acid 437 to about amino acid 440, from about amino acid 508 to about amino acid 511, from about amino acid 515 to about amino acid 518, from about amino acid

516 to about amino acid 519 and from about amino acid 534 to about amino acid 537, and cadherin extracellular repeated domain signature sequences from about amino acid 136 to about amino acid 146 and from about amino acid 244 to about amino acid 254. Clone UNQ478 (DNA53906-1368) has been deposited with ATCC on April 7, 1998 and is assigned ATCC deposit no. 209747.

Analysis of the amino acid sequence of the full-length PRO941 polypeptide suggests that it possesses significant sequence similarity to a cadherin protein, thereby indicating that PRO941 may be a novel cadherin protein family member. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO941 amino acid sequence and the following Dayhoff sequences, I50180, CADA\_CHICK, I50178, GEN12782, CADC\_HUMAN, P\_W25637, A38992, P\_R49731, D38992 and G02678.

#### EXAMPLE 44: Isolation of cDNA Clones Encoding Human PRO944

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA47374. A variety of proprietary Genentech EST sequences were employed in the assembly and are shown in Figures 99-107. Based on the DNA47374 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO944.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CGAGCGAGTCATGGCCAACGC-3' (SEQ ID NO:280)

reverse PCR primer 5'-GTGTCACACGTAGTCTTTCCCGCTGG-3' (SEQ ID NO:281)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47374 sequence which had the following nucleotide sequence

hybridization probe

5'-CTGCAGCTGTTGGGCTTCATTCTCGCCTTCCTGGGATGGATCG-3' (SEQ ID NO:282)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO944 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO944 [herein designated as UNQ481 (DNA52185-1370)] (SEQ ID NO:269) and the derived protein sequence for PRO944.

The entire nucleotide sequence of UNQ481 (DNA52185-1370) is shown in Figure 97 (SEQ ID NO:269). Clone UNQ481 (DNA52185-1370) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 219-221 and ending at the stop codon at nucleotide positions 852-854 (Figure 97). The predicted polypeptide precursor is 211 amino acids long (Figure 98). The full-length PRO944

protein shown in Figure 98 has an estimated molecular weight of about 22,744 daltons and a pI of about 8.51. Analysis of the full-length PRO944 sequence shown in Figure 98 (SEQ ID NO:270) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, transmembrane domains from about amino acid 82 to about amino acid 102, from about amino acid 118 to about amino acid 142 and from about amino acid 161 to about amino acid 187, a potential N-glycosylation site from about amino acid 72 to about amino acid 75, a sequence block having homology to PMP-22/EMP/MP20 family of proteins from about amino acid 70 to about amino acid 111 and a sequence block having homology to ABC-2 type transport system integral membrane protein from about amino acid 119 to about amino acid 133. Clone UNQ481 (DNA52185-1370) has been deposited with ATCC on May 14, 1998 and is assigned ATCC deposit no. 209861.

Analysis of the amino acid sequence of the full-length PRO944 polypeptide suggests that it possesses significant sequence similarity to the CPE-R protein, thereby indicating that PRO944 may be a novel CPE-R homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO944 amino acid sequence and the following Dayhoff sequences, AB000713\_1, AB000714\_1, AF035814\_1, AF000959\_1, HSU89916\_1, EMP2\_HUMAN, JC5732, CELF53B3\_6, PM22\_MOUSE and CGU49797\_1.

#### EXAMPLE 45: Isolation of cDNA Clones Encoding Human PRO983

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA47473. Various proprietary Genentech EST sequences were employed in the assembly, wherein those EST sequences are shown in Figures 110-116. Based on the DNA47473 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO983.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCACCACCGTAGGTACTTGTGTGAGGC-3' (SEQ ID NO:292)

reverse PCR primer 5'-AACCACCAGAGCCAAGAGCCGGG-3' (SEQ ID NO:293)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47473 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGCGGAATCATCGATGCAGGGGCCTCAATTAATGTATCTGTGATGTTAC-3' (SEQ ID NO:294)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO983 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow (LIB256).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO983 [herein designated as UNQ484 (DNA53977-1371)] (SEQ ID NO:283) and the derived protein sequence for PRO983.

The entire nucleotide sequence of UNQ484 (DNA53977-1371) is shown in Figure 108 (SEQ ID NO:283). Clone UNQ484 (DNA53977-1371) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 234-236 and ending at the stop codon at nucleotide positions 963-965 (Figure 108). The predicted polypeptide precursor is 243 amino acids long (Figure 109). The full-length PRO983 protein shown in Figure 109 has an estimated molecular weight of about 27,228 daltons and a pI of about 7.43. Analysis of the full-length PRO983 sequence shown in Figure 109 (SEQ ID NO:284) evidences the presence of the following features: a putative transmembrane domain from about amino acid 224 to about amino acid 239; a potential N-glycosylation site from about amino acid 68 to about amino acid 71; and three potential N-myristoylation sites from about amino acid 59 to about amino acid 64, from about amino acid 64 to about amino acid 69, and from about amino acid 235 to about amino acid 240. Clone UNQ484 (DNA53977-1371) has been deposited with ATCC on May 14, 1998 and is assigned ATCC deposit no. 209862.

Analysis of the amino acid sequence of the full-length PRO983 polypeptide suggests that it possesses significant sequence similarity to the vesicle-associated protein, VAP-33, thereby indicating that PRO983 may be a novel vesicle associated membrane protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO983 amino acid sequence and the following Dayhoff sequences: VP33\_APLCA, CELF33D11\_12, CELF42G2\_2, S50623, YDFC\_SCHPO, CELF54H5\_2, CELZC196\_8, CEF57A10\_3, MSP3\_GLORO, CEC15H11\_1.

#### EXAMPLE 46: Isolation of cDNA Clones Encoding Human PRO1057

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA49808. Based on the DNA49808 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1057.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCATCTGCAGGAGAGAGCGAAGGG-3' (SEQ ID NO:297)

reverse PCR primer 5'-CATCGTTCCCGTGAATCCAGAGGC-3' (SEQ ID NO:298)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA49808 sequence which had the following nucleotide sequence

hybridization probe

5'-GAAGGGAGGCCCTTCCTTTCAGTGGACCCGGGTCAAGAATACCCAC-3' (SEQ ID NO:299)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1057 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1057 [herein designated as UNQ522 (DNA57253-1382)] (SEQ ID NO:295) and the derived protein

sequence for PRO1057.

The entire nucleotide sequence of UNQ522 (DNA57253-1382) is shown in Figure 117 (SEQ ID NO:295). Clone UNQ522 (DNA57253-1382) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 275-277 and ending at the stop codon at nucleotide positions 1514-1516 (Figure 117). The predicted polypeptide precursor is 413 amino acids long (Figure 118). The full-length PRO1057 protein shown in Figure 118 has an estimated molecular weight of about 47,070 daltons and a pI of about 9.92. Analysis of the full-length PRO1057 sequence shown in Figure 118 (SEQ ID NO:296) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, potential N-glycosylation sites from about amino acid 90 to about amino acid 93, from about amino acid 110 to about amino acid 113 and from about amino acid 193 to about amino acid 196, a glycosaminoglycan attachment site from about amino acid 236 to about amino acid 239 and a serine protease histidine-containing active site from about amino acid 165 to about amino acid 170. Clone UNQ522 (DNA57253-1382) has been deposited with ATCC on May 14, 1998 and is assigned ATCC deposit no. 209867.

Analysis of the amino acid sequence of the full-length PRO1057 polypeptide suggests that it possesses significant sequence similarity to various protease proteins, thereby indicating that PRO1057 may be a novel protease. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1057 amino acid sequence and the following Dayhoff sequences, TRYE\_DROER, P\_R14159, A69660, EBN1\_EBV, S65494, GEN12688, A51084\_1, P\_R99571, A57514 and AF003200\_1.

#### 20 EXAMPLE 47: Isolation of cDNA Clones Encoding Human PRO1071

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above. wherein the consensus sequence obtained is herein designated DNA53035. Based on the DNA53035 consensus sequence, it was determined that that consensus sequence shared significant sequence identity with Incyte EST clone no. 2872569, a clone that upon review appeared to encode a full length protein. As such, Incyte EST clone no. 2872569 was purchased and its insert was obtained and sequenced so as to confirm the proper sequence. This sequence is herein designated UNQ528 or DNA58847-1383.

DNA sequencing of the clone isolated as described above gave the full-length DNA sequence for PRO1071 [herein designated as UNQ528 (DNA58847-1383)] (SEQ ID NO:300) and the derived protein sequence for PRO1071.

The entire nucleotide sequence of UNQ528 (DNA58847-1383) is shown in Figure 119 (SEQ ID NO:300). Clone UNQ528 (DNA58848-1383) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 133-135 and ending at the stop codon at nucleotide positions 1708-1710 (Figure 119). The predicted polypeptide precursor is 525 amino acids long (Figure 120). The full-length PRO1071 protein shown in Figure 120 has an estimated molecular weight of about 58,416 daltons and a pI of about 6.62. Analysis of the full-length PRO1071 sequence shown in Figure 120 (SEQ ID NO:301) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, a potential N-

glycosylation site from about amino acid 251 to about amino acid 254, a thrombospondin-1 homology block from about amino acid 385 to about amino acid 399 and von Willibrands factor type C homology blocks from about amino acid 385 to about amino acid 399, from about amino acid 445 to about amino acid 459 and from about amino acid 42 to about amino acid 56. Clone UNQ528 (DNA58847-1383) has been deposited with ATCC on May 20, 1998 and is assigned ATCC deposit no. 209879.

5 Analysis of the amino acid sequence of the full-length PRO1071 polypeptide suggests that it possesses significant sequence similarity to the thrombospondin protein, thereby indicating that PRO1071 may be a novel thrombospondin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1071 amino acid sequence and the following Dayhoff sequences, AB002364\_1, D67076\_1, BTPCINPGN\_1, CET13H10\_1, CEF25H8\_5, CEF53B6\_2, CEC26C6\_6,  
10 HSSEMG\_1, CET21B6\_4 and BTY08561\_1.

#### EXAMPLE 48: Isolation of cDNA Clones Encoding Human PRO1072

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA53125. Based on the DNA53125  
15 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1072.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCAGGAAATGCTCCAGGAAGAGCC-3' (SEQ ID NO:305)

20 reverse PCR primer 5'-GCCCATGACACCAAATTGAAGAGTGG-3' (SEQ ID NO:306)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA53125 sequence which had the following nucleotide sequence

hybridization probe

5'-AACGCAGGGATCTTCCAGTGCCCTTACATGAAGACTGAAGATGGG-3' (SEQ ID NO:307)

25 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1072 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB26).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for  
30 PRO1072 [herein designated as UNQ529 (DNA58747-1384)] (SEQ ID NO:302) and the derived protein sequence for PRO1072.

The entire nucleotide sequence of UNQ529 (DNA58747-1384) is shown in Figure 121 (SEQ ID NO:302). Clone UNQ529 (DNA58747-1384) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 65-67 and ending at the stop codon at nucleotide positions 1073-1075  
35 (Figure 121). The predicted polypeptide precursor is 336 amino acids long (Figure 122). The full-length PRO1072 protein shown in Figure 122 has an estimated molecular weight of about 36,865 daltons and a pI of

about 9.15. Analysis of the full-length PRO1072 sequence shown in Figure 122 (SEQ ID NO:303) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, short-chain alcohol dehydrogenase protein homology blocks from about amino acid 134 to about amino acid 144, from about amino acid 44 to about amino acid 56 and from about amino acid 239 to about amino acid 248 and potential N-glycosylation sites from about amino acid 212 to about amino acid 215 and from about amino acid 239 to about amino acid 242. Clone UNQ529 (DNA58747-1384) has been deposited with ATCC on May 14, 1998 and is assigned ATCC deposit no. 209868.

Analysis of the amino acid sequence of the full-length PRO1072 polypeptide suggests that it possesses significant sequence similarity to the reductase family of proteins, thereby indicating that PRO1072 may be a novel reductase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1072 amino acid sequence and the following Dayhoff sequences, P\_W03198, P\_W15759, P\_R60800, MTV037\_3, CEC15H11\_6, ATAC00234314, MTV022\_13, SCU43704\_1, OXIR\_STRAT AND CELC01G8\_3.

#### 15 EXAMPLE 49: Isolation of cDNA Clones Encoding Human PRO1075

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA34363. Based on the DNA34363 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1075.

20 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGAGAGGCCTCTCTGGAAGTTG-3' (SEQ ID NO:312)

forward PCR primer 5'-GTCACCGATCACTGAAAGC-3' (SEQ ID NO:313)

forward PCR primer 5'-CCAGAATGAAGTAGCTCGGC-3' (SEQ ID NO:314)

forward PCR primer 5'-CCGACTCAAATGCATTGTC-3' (SEQ ID NO:315)

25 forward PCR primer 5'-CATTTGGCAGGAATTGTCC-3' (SEQ ID NO:316)

forward PCR primer 5'-GGTGCTATAGGCCAAGGG-3' (SEQ ID NO:317)

reverse PCR primer 5'-CTGTATCTCTGGGCTATGTCAGAG-3' (SEQ ID NO:318)

reverse PCR primer 5'-CTACATATAATGGCACATGTCAGCC-3' (SEQ ID NO:319)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA34363 sequence which had the following nucleotide sequence

hybridization probe

5'-CGTCTTCCTATCCTTACCCGACCTCAGATGCTCCCTTCTGCTCCTG-3' (SEQ ID NO:320)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1075 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human skin tumor tissue (LIB324).



DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1075 [herein designated as UNQ532 (DNA57689-1385)] (SEQ ID NO:308) and the derived protein sequence for PRO1075.

The entire nucleotide sequence of UNQ532 (DNA57689-1385) is shown in Figure 124 (SEQ ID NO:308). Clone UNQ532 (DNA57689-1385) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 137-139 and ending at the stop codon at nucleotide positions 1355-1357 (Figure 124). The predicted polypeptide precursor is 406 amino acids long (Figure 125). The full-length PRO1075 protein shown in Figure 125 has an estimated molecular weight of about 46,927 daltons and a pI of about 5.21. Analysis of the full-length PRO1075 sequence shown in Figure 125 (SEQ ID NO:309) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 29, an endoplasmic reticulum targeting sequence from about amino acid 403 to about amino acid 406, a tyrosine kinase phosphorylation site from about amino acid 203 to about amino acid 211 and a sequence block having homology to the thioredoxin family of proteins from about amino acid 50 to about amino acid 66. Clone UNQ532 (DNA57689-1385) has been deposited with ATCC on May 14, 1998 and is assigned ATCC deposit no. 209869.

Analysis of the amino acid sequence of the full-length PRO1075 polypeptide suggests that it possesses significant sequence similarity to protein disulfide isomerase, thereby indicating that PRO1075 may be a novel protein disulfide isomerase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1075 amino acid sequence and the following Dayhoff sequences, CELC30H7\_2, CELC06A6\_3, CELF42G8\_3, S57942, ER72\_CAEEL, CELC07A12\_3, CEH06O01\_4 and P\_R51696.

#### EXAMPLE 50: Isolation of cDNA Clones Encoding Human PRO181

A cDNA sequence isolated in the amylose screen described in Example 2 above was found, by BLAST and FastA sequence alignment, to have sequence homology to a nucleotide sequence encoding the cornichon protein. This cDNA sequence is herein designated DNA13242 (Figure 130; SEQ ID NO:323). Based on the sequence homology, oligonucleotide probes were generated from the sequence of the DNA13242 molecule and used to screen a human placenta (LIB89) library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed included:

forward PCR primer 5'-GTGCAGCAGAGTGGCTTACA-3' (SEQ ID NO:326)

reverse PCR primer 5'-ACTGGACCAATTCTTCTGTG-3' (SEQ ID NO:327)

hybridization probe

5'-GATATTCTAGCATATTGTCAGAAGGAAGGATGGTGCAAATTAGCT-3' (SEQ ID NO:328)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 14-16 and ending at the stop codon found at nucleotide positions 446-448 (Figure 128; SEQ ID NO:321). The predicted polypeptide precursor is 144 amino acids long, has a

calculated molecular weight of approximately 16,699 daltons and an estimated pI of approximately 5.6. Analysis of the full-length PRO181 sequence shown in Figure 129 (SEQ ID NO:322) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, a putative type II transmembrane domain from about amino acid 11 to about amino acid 31 and other transmembrane domains from about amino acid 57 to about amino acid 77 and from about amino acid 123 to about amino acid 143. Clone UNQ155  
 5 (DNA23330-1390) has been deposited with ATCC on April 14, 1998 and is assigned ATCC deposit no. 209775.

Analysis of the amino acid sequence of the full-length PRO181 polypeptide suggests that it possesses significant sequence similarity to the cornichon protein, thereby indicating that PRO181 may be a novel cornichon homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO181 amino acid sequence and the following Dayhoff sequences,  
 10 AF022811\_1, CET09E8\_3, S64058, YGF4\_YEAST, YB60\_YEAST, EBU89455\_1, SIU36383\_3 and PH1371.

#### EXAMPLE 51: Isolation of cDNA Clones Encoding Human PRO195

A cDNA sequence was isolated in the amylase screen described in Example 2 above and is herein designated DNA13199 (Figure 134; SEQ ID NO:332). The DNA13199 sequence was then compared to a  
 15 variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington,  
 20 Seattle, Washington; <http://bozeman.mbt.washington.edu/phrap.docs/phrap.html>). The consensus sequence obtained therefrom is herein designated as DNA22778.

Based on the DNA22778 sequence, oligonucleotide probes were generated and used to screen a human placenta library (LIB89) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science,  
 25 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-ACAAGCTGAGCTGCTGTGACAG-3' (SEQ ID NO:333)

reverse PCR primer 5'-TGATTCTGGCAACCAAGATGGC-3' (SEQ ID NO:334)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA22778 sequence  
 30 which had the following nucleotide sequence

hybridization probe

5'-ATGGCCTTGCCCGGAGGTTCGGGGACCGCTTCGGCTGAAG-3' (SEQ ID NO:335)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to  
 35 isolate clones encoding the PRO195 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent

translational initiation site at nucleotide positions 70-72 and ending at the stop codon found at nucleotide positions 1039-1041 (Figure 132; SEQ ID NO:330). The predicted polypeptide precursor is 323 amino acids long, has a calculated molecular weight of approximately 36,223 daltons and an estimated pI of approximately 5.06. Analysis of the full-length PRO195 sequence shown in Figure 132 (SEQ ID NO:330) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31, a transmembrane domain from about amino acid 241 to about amino acid 260 and a potential N-glycosylation site from about amino acid 90 to about amino acid 93. Clone UNQ169 (DNA26847-1395) has been deposited with ATCC on April 14, 1998 and is assigned ATCC deposit no. 209772.

Analysis of the amino acid sequence of the full-length PRO195 polypeptide suggests that it possesses no significant sequence similarity to any known protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO195 amino acid sequence and the following Dayhoff sequences, P\_P91380, AF035118\_1, HUMTROPES\_1, NUOD\_SALTY and E70002.

#### EXAMPLE 52: Isolation of cDNA Clones Encoding Human PRO865

A cDNA sequence isolated in the amylase screen described in Example 2 above was herein designated DNA37642 (Figure 137, SEQ ID NO:338). The DNA37642 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologies therebetween. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington; <http://ccr.biology.washington.edu/phrap/docs/phrap.html>). The consensus sequence obtained is herein designated DNA48615.

Based on the DNA48615 consensus sequence, probes were generated and used to screen a human fetal kidney (LIB227) library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 1 5'-AAGCTGCCGAGCTGCAATG-3' (SEQ ID NO:339)

forward PCR primer 2 5'-TTGCTTCTTAATCCTGAGCGC-3' (SEQ ID NO:340)

forward PCR primer 3 5'-AAAGGAGGACTTTCGACTGC-3' (SEQ ID NO:341)

reverse PCR primer 1 5'-AGAGATTCATCCACTGCTCCAAGTCG-3' (SEQ ID NO:342)

reverse PCR primer 2 5'-TGTCCAGAAACAGGCACATATCAGC-3' (SEQ ID NO:343)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA48615 sequence which had the following nucleotide sequence

hybridization probe

5'-AGACAGCGGCACAGAGGTGCTTCTGCCAGGTTAGTGGTTACTTGGATGAT-3' (SEQ ID NO:344)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO865 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent  
 5 translational initiation site at nucleotide positions 173-175 and ending at the stop codon found at nucleotide  
 positions 1577-1579 (Figure 135; SEQ ID NO:336). The predicted polypeptide precursor is 468 amino acids  
 long, has a calculated molecular weight of approximately 54,393 daltons and an estimated pI of approximately  
 5.63. Analysis of the full-length PRO865 sequence shown in Figure 136 (SEQ ID NO:337) evidences the  
 presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, potential N-  
 10 glycosylation sites from about amino acid 280 to about amino acid 283 and from about amino acid 384 to about  
 amino acid 387, a potential amidation site from about amino acid 94 to about amino acid 97, glycosaminoglycan  
 attachment sites from about amino acid 20 to about amino acid 23 and from about amino acid 223 to about amino  
 acid 226, an aminotransferase class-V pyridoxyl-phosphate amino acid sequence block from about amino acid  
 216 to about amino acid 222 and an amino acid sequence block similar to that found in the interleukin-7 protein  
 15 from about amino acid 338 to about amino acid 343. Clone UNQ434 (DNA53974-1401) has been deposited with  
 ATCC on April 14, 1998 and is assigned ATCC deposit no. 209774.

Analysis of the amino acid sequence of the full-length PRO865 polypeptide suggests that it possesses  
 no significant sequence similarity to any known protein. However, an analysis of the Dayhoff database (version  
 35.45 SwissProt 35) evidenced some degree of homology between the PRO865 amino acid sequence and the  
 20 following Dayhoff sequences, YMNO\_YEAST, ATFCA4\_43, S44168, P\_W14549 and RABTCRG4\_1.

#### EXAMPLE 33: Isolation of cDNA Clones Encoding Human PRO827

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by BLAST  
 and FastA sequence alignment, to have sequence homology to nucleotide sequences encoding various integrin  
 25 proteins. This cDNA sequence is herein designated DNA47751 (see Figure 140; SEQ ID NO:347). Based on  
 the sequence homology, probes were generated from the sequence of the DNA47751 molecule and used to screen  
 a human fetal pigment epithelium library (LIB113) prepared as described in paragraph 1 of Example 2 above.  
 The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes  
 et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

30 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGGGACAGAGGCCAGAGGACTTC-3' (SEQ ID NO:348)

reverse PCR primer 5'-CAGGTGCATATTCACAGCAGGATG-3' (SEQ ID NO:349)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47751  
 sequence which had the following nucleotide sequence

35 hybridization probe

5'-GGAACCTCCCCTTCGTCACTCACCTGTTCTTGCCCCTGGTGTTCCT-3' (SEQ ID

NO:350)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO827 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent  
5 translational initiation site at nucleotide positions 134-136 and ending at the stop codon found at nucleotide positions 506-508 (Figure 138; SEQ ID NO:345). The predicted polypeptide precursor is 124 amino acids long, has a calculated molecular weight of approximately 13,352 daltons and an estimated pI of approximately 5.99. Analysis of the full-length PRO827 sequence shown in Figure 139 (SEQ ID NO:346) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 22, a cell attachment sequence from  
10 about amino acid 70 to about amino acid 72, a potential N-glycosylation site from about amino acid 98 to about amino acid 101 and an integrin alpha chain protein homology sequence from about amino acid 67 to about amino acid 81. Clone UNQ468 (DNA57039-1402) has been deposited with ATCC on April 14, 1998 and is assigned ATCC deposit no. 209777.

Analysis of the amino acid sequence of the full-length PRO827 polypeptide suggests that it possesses  
15 significant sequence similarity to the VLA-2 integrin protein and various other integrin proteins, thereby indicating that PRO827 may be a novel integrin or splice variant thereof. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO240 amino acid sequence and the following Dayhoff sequences, S44142, ITA2\_HUMAN, ITA1\_RAT, ITA1\_HUMAN, ITA4\_HUMAN, ITA9\_HUMAN, AF032108\_1, ITAM\_MOUSE, ITA8\_CHICK and ITA6\_CHICK.

20

#### EXAMPLE 54: Isolation of cDNA Clones Encoding Human PRO1114

A cDNA sequence isolated in the amylose screen described in Example 2 was found, by the WU-BLAST2 sequence alignment computer program, to have certain sequence identity to other known interferon  
25 receptors. This cDNA sequence is herein designated DNA48466 (Figure 143; SEQ ID NO:352). Based on the sequence identity, probes were generated from the sequence of the DNA48466 molecule and used to screen a human breast carcinoma library (LIB135) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

30 forward PCR primer 5'-AGGCTTCGCTGCGACTAGACCTC-3' (SEQ ID NO:354)  
reverse PCR primer 5'-CCAGGTCGGGTAAGGATGGTTGAG-3' (SEQ ID NO:355)  
hybridization probe

5'-TTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC-3' (SEQ ID NO:356)

A full length clone was identified that contained a single open reading frame with an apparent  
35 translational initiation site at nucleotide positions 250-252, and a stop signal at nucleotide positions 1183-1185 (Figure 141, SEQ ID NO:351). The predicted polypeptide precursor is 311 amino acids long, has a calculated

molecular weight of approximately 35,076 daltons and an estimated pI of approximately 5.04. Analysis of the full-length PRO1114 interferon receptor sequence shown in Figure 142 (SEQ ID NO:352) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 29, a transmembrane domain from about amino acid 230 to about amino acid 255, potential N-glycosylation sites from about amino acid 40 to about amino acid 43 and from about amino acid 134 to about amino acid 137, an amino acid sequence block having homology to tissue factor proteins from about amino acid 92 to about amino acid 119 and an amino acid sequence block having homology to integrin alpha chain proteins from about amino acid 232 to about amino acid 262. Clone UNQ557 (DNA57033-1403) has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209905.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 142 (SEQ ID NO:352), evidenced significant homology between the PRO1114 interferon receptor amino acid sequence and the following Dayhoff sequences: G01418, INR1\_MOUSE, P\_R71035, INGS\_HUMAN, A26595\_1, A26593\_1, I56215 and TF\_HUMAN.

#### EXAMPLE 55: Isolation of cDNA Clones Encoding Human PRO237

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA30905. Based on the DNA30905 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO237.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TCTGCTGAGGTGCAGCTCATTAC-3' (SEQ ID NO:359)

reverse PCR primer 5'-GAGGCTCTGGAAGATCTGAGATGG-3' (SEQ ID NO:360)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA30905 sequence which had the following nucleotide sequence

hybridization probe

5'-GCCTCTTTGTCAACGTTGCCAGTACCTCTAACCCATTCCTCAGTCGCCTC-3' (SEQ ID NO:361)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO237 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue (LIB153).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO237 [herein designated as UNQ211 (DNA34353-1428)] (SEQ ID NO:357) and the derived protein sequence for PRO237.

The entire nucleotide sequence of UNQ211 (DNA34353-1428) is shown in Figure 144 (SEQ ID NO:357). Clone UNQ211 (DNA34353-1428) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 586-588 and ending at the stop codon at nucleotide positions 1570-1572

(Figure 144). The predicted polypeptide precursor is 328 amino acids long (Figure 145). The full-length PRO237 protein shown in Figure 145 has an estimated molecular weight of about 36,238 daltons and a pI of about 9.90. Analysis of the full-length PRO237 sequence shown in Figure 145 (SEQ ID NO:358) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a transmembrane domain from about amino acid 177 to about amino acid 199, potential N-glycosylation sites from about amino acid 118 to about amino acid 121, from about amino acid 170 to about amino acid 173 and from about amino acid 260 to about amino acid 263 and eukaryotic-type carbonic anhydrase sequence homology blocks from about amino acid 222 to about amino acid 270, from about amino acid 128 to about amino acid 164 and from about amino acid 45 to about amino acid 92. Clone UNQ211 (DNA34353-1428) has been deposited with ATCC on May 12, 1998 and is assigned ATCC deposit no. 209855.

Analysis of the amino acid sequence of the full-length PRO237 polypeptide suggests that it possesses significant sequence similarity to the carbonic anhydrase protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO237 amino acid sequence and the following Dayhoff sequences, AF050106\_1, OACALP\_1, CELD1022\_8, CAH2\_HUMAN, ICAC, CAH5\_HUMAN, CAHP\_HUMAN, CAH3\_HUMAN, CAH1\_HUMAN and 2CAB.

#### EXAMPLE 56: Isolation of cDNA Clones Encoding Human PRO541

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42259. Based on the DNA42259 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO541.

~~PCR primers (forward and reverse) were synthesized:~~

forward PCR primer 5'-GGACAGAATTTGGGAGCACACTGG-3' (SEQ ID NO:364)

forward PCR primer 5'-CCAAGAGTATACTGTCCTCG-3' (SEQ ID NO:365)

reverse PCR primer 5'-AGCACAGATTTTCTCTACAGCCCCC-3' (SEQ ID NO:366)

reverse PCR primer 5'-AACCACTCCAGCATGTACTGCTGC-3' (SEQ ID NO:367)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42259 sequence which had the following nucleotide sequence

hybridization probe

5'-CCATTCAGGTGTTCTGGCCCTGTATGTACACATTATACACAGGTCGTGTG-3' (SEQ ID NO:368)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO541 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO541 [herein designated as UNQ342 (DNA45417-1432)] (SEQ ID NO:362) and the derived protein sequence

for PRO541.

The entire nucleotide sequence of UNQ342 (DNA45417-1432) is shown in Figure 146 (SEQ ID NO:362). Clone UNQ342 (DNA45417-1432) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 469-471 and ending at the stop codon at nucleotide positions 1969-1971 (Figure 146). The predicted polypeptide precursor is 500 amino acids long (Figure 147). The full-length PRO541 protein shown in Figure 147 has an estimated molecular weight of about 56,888 daltons and a pI of about 8.53. Analysis of the full-length PRO541 sequence shown in Figure 147 (SEQ ID NO:363) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, amino acid sequence blocks having homology to extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 from about amino acid 165 to about amino acid 186, from about amino acid 196 to about amino acid 218, from about amino acid 134 to about amino acid 146, from about amino acid 96 to about amino acid 108 and from about amino acid 58 to about amino acid 77 and a potential N-glycosylation site from about amino acid 28 to about amino acid 31. Clone UNQ342 (DNA45417-1432) has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209910.

Analysis of the amino acid sequence of the full-length PRO541 polypeptide suggests that it possesses significant sequence similarity to a trypsin inhibitor protein, thereby indicating that PRO541 may be a novel trypsin inhibitor. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO541 amino acid sequence and the following Dayhoff sequences, D45027\_1, AB009609\_1, JC5308, CRS3\_HORSE, TPX1\_HUMAN, HELO\_HELHO, GEN14351, A28112\_1, CET05A10\_4 and P\_W11485.

#### EXAMPLE 57: Isolation of cDNA Clones Encoding Human PRO273

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above. From the consensus sequence obtained is herein designated DNA36465. Based on the DNA36465 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO273.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CAGCGCCCTCCCCATGTCCCTG-3' (SEQ ID NO:371)

reverse PCR primer 5'-TCCCAACTGGTTTGGAGTTTCCC-3' (SEQ ID NO:372)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36465 sequence which had the following nucleotide sequence

hybridization probe

5'-CTCCGGTCAGCATGAGGCTCCTGGCGGCCGCTGCTCCTGCTGCTG-3' (SEQ ID NO:373)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO273 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.



DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO273 [herein designated as UNQ240 (DNA39523-1192)] (SEQ ID NO:369) and the derived protein sequence for PRO273.

The entire nucleotide sequence of UNQ240 (DNA39523-1192) is shown in Figure 148 (SEQ ID NO:369). Clone UNQ240 (DNA39523-1192) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 167-169 and ending at the stop codon at nucleotide positions 500-502 (Figure 148). The predicted polypeptide precursor is 111 amino acids long (Figure 149). Clone UNQ240 (DNA39523-1192) has been deposited with the ATCC. It is understood that the deposited clone contains the actual sequence and that the sequences provided herein are merely representative based on current sequencing techniques. Moreover, given the sequences provided herein and knowledge of the universal genetic code, the corresponding nucleotides for any given amino acid can be routinely identified and vice versa.

Analysis of the amino acid sequence of the full-length PRO273 polypeptide suggests that portions of it possess sequence identity with human macrophage inflammatory protein-2, cytokine-induced neutrophil chemoattractant 2, and neutrophil chemotactic factor 2-beta, thereby indicating that PRO273 is a novel chemokine.

As discussed further below, the cDNA was subcloned into a baculovirus vector and expressed in insect cells as a C-terminally tagged IgG fusion protein. N-terminal sequencing of the resultant protein identified the signal sequence cleavage site, yielding a mature polypeptide of 77 amino acids. The mature sequence, showing 31-40% identity to other human CXC chemokines, includes the four canonical cysteine residues but lacks the ELR motif. Northern analysis demonstrates expression at least in the small intestine, colon, spleen, lymph node and kidney. By in situ hybridization, also described in detail below, mRNA is localized to the lamina propria of intestinal villi and to renal tubules.

#### EXAMPLE 58: Isolation of cDNA Clones Encoding Human PRO701

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39848. Based on the DNA39848 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO701.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GGCAAGCTACGGAACGTCATCGTG-3' (SEQ ID NO:376)

reverse PCR primer 5'-AACCCCGAGCCAAAAGATGGTCAC-3' (SEQ ID NO:377)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39848 sequence which had the following nucleotide sequence:

hybridization probe

5'-GTACCGGTGACCAGGCAGCAAAAGGCAACTATGGGCTCCTGGATCAG-3' (SEQ ID NO:378).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO701 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO701 [herein designated as UNQ365 (DNA44205-1285)] (SEQ ID NO:374) and the derived protein sequence for PRO701.

The entire nucleotide sequence of UNQ365 (DNA44205-1285) is shown in Figure 150 (SEQ ID NO:374). Clone UNQ365 (DNA44205-1285) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 50-52 and ending at the stop codon at nucleotide positions 2498-3000 (Figure 150). The predicted polypeptide precursor is 816 amino acids long (Figure 151). The full-length PRO701 protein shown in Figure 151 has an estimated molecular weight of about 91,794 daltons, a pI of about 5.88 and NX(S/T) being 4. Clone UNQ365 (DNA44205-1285) has been deposited with the ATCC on March 31, 1998. It is understood that the clone was the correct and actual sequence, wherein the sequences provided herein are representative based on sequencing techniques.

Still regarding the amino acid sequence shown in Figure 151, there is a potential signal peptide cleavage site at about amino acid 25. There are potential N-glycosylation sites at about amino acid positions 83, 511, 716 and 803. The carboxylesterases type-B signature 2 sequence is at about residues 125 to 135. Regions homologous with carboxylesterase type-B are also at about residues 54-74, 197-212 and 221-261. A potential transmembrane region corresponds approximately to amino acids 671 through about 700. The corresponding nucleic acids can be routinely determined from the sequences provided herein.

Analysis of the amino acid sequence of the full-length PRO701 polypeptide suggests that it possess significant homology to the neuroligins from *rattus norvegicus* indicating that PRO701 may be a novel human

#### EXAMPLE 59: Isolation of cDNA Clones Encoding Human PRO704

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43033. Based on the DNA43033 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO704.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTTGGGTCGTGGCAGCAGTGG-3' (SEQ ID NO:381);

reverse PCR primer 5'-CACTCTCCAGGCTGCATGCTCAGG-3' (SEQ ID NO:382).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43033 consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-GTCAAACGTTTCGAGTACTTGAAACGGGAGCACTCGCTGTCGAAGC-3' (SEQ ID NO:383).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO704 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO704 [herein designated as UNQ368 (DNA50911-1288)] (SEQ ID NO:379) and the derived protein sequence for PRO704.

The entire nucleotide sequence of UNQ368 (DNA50911-1288) is shown in Figure 152 (SEQ ID NO:379). Clone UNQ368 (DNA50911-1288) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 8-10 and ending at the stop codon at nucleotide positions 1052-1054 (Figure 152). The predicted polypeptide precursor is 348 amino acids long (Figure 153). The full-length PRO704 protein shown in Figure 153 has an estimated molecular weight of about 39,711 and a pI of about 8.7. Clone UNQ368 (DNA50911-1288) has been deposited with the ATCC on March 31, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO704 polypeptide suggests that portions of it possess significant homology to the vesicular integral membrane protein 36, thereby indicating that PRO704 may be a novel vesicular integral membrane protein.

Still analyzing the amino acid sequence of SEQ ID NO:380, the putative signal peptide is at about amino acids 1-39 of SEQ ID NO:380. The transmembrane domain is at amino acids 310-335 of SEQ ID NO:380. A potential N-glycosylation site is at about amino acids 180-183 of SEQ ID NO:380. The corresponding nucleotides can be routinely determined given the sequences provided herein.

#### EXAMPLE 60: Isolation of cDNA Clones Encoding Human PRO706

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA40669. Based on the DNA40669 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO706.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCAAGCAGCTTAGAGCTCCAGACC-3' (SEQ ID NO:386)

reverse PCR primer 5'-TTCCCTATGCTCTGTATTGGCATGG-3' (SEQ ID NO:387)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40669 sequence which had the following nucleotide sequence

hybridization probe

5'-GCCACTTCTGCCACAATGTCAGCTTTCCTGTACCAGAAATGGCTGTGTT-3' (SEQ ID NO:388)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO706 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue (LIB153).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO706 [herein designated as UNQ370 (DNA48329-1290)] (SEQ ID NO:384) and the derived protein sequence for PRO706. It is understood that the deposited clone contains the actual sequence, and that the sequences provided herein are representative based on current sequencing techniques.

The entire nucleotide sequence of UNQ370 (DNA48329-1290) is shown in Figure 154 (SEQ ID NO:384). Clone UNQ370 (DNA48329-1290) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 279-281 and ending at the stop codon at nucleotide positions 1719-1721 (Figure 154). The predicted polypeptide precursor is 480 amino acids long (Figure 155). The full-length PRO706 protein shown in Figure 155 has an estimated molecular weight of about 55,239 daltons and a pI of about 9.30. Clone UNQ370 (DNA48329-1290) has been deposited with the ATCC on April 21, 1998.

Still regarding the amino acid sequence shown in Figure 155, there is a potential signal peptide cleavage site at about amino acid 19. There are potential N-glycosylation sites at about amino acid positions 305 and 354. There is a potential tyrosine kinase phosphorylation site at about amino acid position 333. A region homologous with histidine acid phosphatase is at about residues 87-102. The corresponding nucleic acid regions can be routinely determined given the provided sequences, i.e., the codons can be determined from the specifically named amino acids given.

Analysis of the amino acid sequence of the full-length PRO706 polypeptide suggests that portions of it possess significant homology to the human prostatic acid phosphatase precursor thereby indicating that PRO706 may be a novel human prostatic acid phosphatase.

#### EXAMPLE 61: Isolation of cDNA Clones Encoding Human PRO707

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42775. Based on DNA42775, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO707.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TCCGTCTCTGTGAACCGCCCCAC-3' (SEQ ID NO:391);

reverse PCR primer 5'-CTCGGGCGCATTGTCGTTCTGGTC-3' (SEQ ID NO:392).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA42775 sequence which had the following nucleotide sequence:

hybridization probe

5'-CCGACTGTGAAAGAGAACGCCCCAGATCCACTTATTCCCC-3' (SEQ ID NO:393).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was

screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO707 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO707 [herein designated as UNQ371 (DNA48306-1291)] (SEQ ID NO:389) and the derived protein sequence for PRO707.

The entire nucleotide sequence of UNQ371 (DNA48306-1291) is shown in Figure 156 (SEQ ID NO:389). Clone UNQ371 (DNA48306-1291) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 371-373 and ending at the stop codon at nucleotide positions 3119-3121 of SEQ ID NO:389. The predicted polypeptide precursor is 916 amino acids long (Figure 157). The full-length PRO707 protein shown in Figure 157 has an estimated molecular weight of about 100,204 daltons and a pI of about 4.92. Clone UNQ371 (DNA48306-1291) has been deposited with ATCC on May 27, 1998. It is understood that the clone UNQ371 which is deposited is that which encodes PRO707, and that the sequences herein are merely representations based on known sequencing techniques which may be subject to minor errors.

Regarding analysis of the amino acid sequence, the signal sequence appears to be at about 1 through 30 of SEQ ID NO:390. Cadherins extracellular repeated domain signature sequence is at about amino acids 121-131, 230-240, 335-345, 440-450, and 550-560 of SEQ ID NO:390. Tyrosine kinase phosphorylation sites are at about amino acids 124-132 and 580-586 of SEQ ID NO:390. A potential transmembrane domain is at about amino acids 682-715  $\pm$  5. The nucleic acid positions can be derived by referring to the corresponding codon for the named amino acid.

Analysis of the amino acid sequence of the full-length PRO707 polypeptide suggests that portions of it possess significant homology to the cadherin FIB3 protein, expressed in human fibroblasts, thereby indicating that PRO707 may be a novel cadherin.

#### EXAMPLE 62: Isolation of cDNA Clones Encoding Human PRO322

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA48336. Based on the DNA48336 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO322.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CAGCCTACAGAATAAAGATGGCCC-3' (SEQ ID NO:396)

reverse PCR primer 5'-GGTGCAATGATCTGCCAGGCTGAT-3' (SEQ ID NO:397)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48336 consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-AGAAATACCTGTGGTTCAGTCCATCCCAAACCCCTGCTACAACAGCAG-3' (SEQ ID NO:398).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO322 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

5 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO322 [herein designated as UNQ283 (DNA48336-1309)] (SEQ ID NO:394) and the derived protein sequence for PRO322. It is understood that UNQ283 (DNA48336-1309) in fact encodes PRO322, and that SEQ ID NO:394 is a representation of the sequence based on sequencing techniques known in the art.

10 The entire nucleotide sequence of UNQ283 (DNA48336-1309) is shown in Figure 158 (SEQ ID NO:394). Clone UNQ283 (DNA48336-1309) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 166-168 and ending at the stop codon at nucleotide positions 946-948 (Figure 158). The predicted polypeptide precursor is 260 amino acids long (Figure 159). The full-length PRO322 protein shown in Figure 159 has an estimated molecular weight of about 28,028 daltons and a pI of about 7.87. Clone UNQ283 (DNA48336-1309) has been deposited with ATCC and is assigned ATCC deposit  
15 no. 209669.

Regarding the amino acid sequence of Figure 159, a potential N-glycosylation site is at amino acid 110 of SEQ ID NO:395. The serine proteases, trypsin family and histidine active site is identified at amino acids 69 through 74 of SEQ ID NO:395 and the consensus sequence is identified at amino acids 207 through 217 of SEQ ID NO:395. The kringle domain proteins motif is identified at amino acids 205 through 217 of SEQ ID  
20 NO:395. The putative signal peptide is encoded at about amino acids 1-23.

Analysis of the amino acid sequence of the full-length PRO322 polypeptide suggests that portions of it possess significant homology to neuropsin and other serine proteases, thereby indicating that PRO322 is a novel serine protease related to neuropsin.

#### 25 EXAMPLE 63: Isolation of cDNA Clones Encoding Human PRO526

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39626. Based on the DNA39626 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for  
30 PRO526.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGGCTGCCCTGCAGTACCTCTACC-3' (SEQ ID NO:401);

reverse PCR primer 5'-CCCTGCAGGTCATTGGCAGCTAGG-3' (SEQ ID NO:402).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA39626 consensus  
35 sequence which had the following nucleotide sequence:

hybridization probe

5'-AGGCACTGCCTGATGACACCTTCCGCGACCTGGGCAACCTCACAC-3' (SEQ ID NO:403).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO526 gene using the probe oligonucleotide and one of the PCR primers. RNA  
5 for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB228).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO526 [herein designated as UNQ330 (DNA44184-1319)] (SEQ ID NO:399) and the derived protein sequence for PRO526.

The entire nucleotide sequence of UNQ330 (DNA44184-1319) is shown in Figure 160 (SEQ ID  
10 NO:399). Clone UNQ330 (DNA44184-1319) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 514-516 and ending at the stop codon at nucleotide positions 1933-1935 (Figure 160). The predicted polypeptide precursor is 473 amino acids long (Figure 161). The full-length PRO526 protein shown in Figure 161 has an estimated molecular weight of about 50,708 daltons and a pI of about 9.28. Clone UNQ330 (DNA44184-1319) has been deposited with the ATCC on March 26, 1998. It is  
15 understood that the clone contains the actual sequence, whereas the sequences presented herein are representative based on current sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO526 polypeptide suggests that portions of it possess significant homology to the leucine repeat rich proteins including ALS, SLIT, carboxypeptidase and platelet glycoprotein V thereby indicating that PRO526 is a novel protein which is involved in protein-protein  
20 interactions.

Still analyzing SEQ ID NO:400, the signal peptide sequence is at about amino acids 1-26. A leucine zipper pattern is at about amino acids 135-156. A glycosaminoglycan attachment is at about amino acids 436-439. N-glycosylation sites are at about amino acids 82-85, 179-182, 237-240 and 423-426. A von Willebrand factor (VWF) type C domain(s) is found at about amino acids 411-425. The skilled artisan can understand  
25 which nucleotides correspond to these amino acids based on the sequences provided herein.

EXAMPLE 64: Isolation of cDNA Clones Encoding Human PRO531

An ECD database was searched and an expressed sequence tag (EST) from LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA was identified which showed homology to protocadherin 3. Based on this  
30 sequence, a search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequence. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington;  
35 <http://bozeman.mbt.washington.edu/phrap.docs/phrap.html>).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. Based on the

consensus sequence obtained, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO531.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTGAGAACGCGCCTGAAACTGTG-3' (SEQ ID NO:406);

5 reverse PCR primer 5'-AGCGTTGTCATTGACATCGGCG-3' (SEQ ID NO:407).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA sequence which had the following nucleotide sequence:

hybridization probe

5'-TTAGTTGCTCCATTCAGGAGGATCTACCCTTCCTCCTGAAATCCGCGGAA-3' (SEQ ID NO:408).

10 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO531 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue (LIB153). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents  
15 such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

20 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO531 [herein designated as UNQ332 (DNA48314-1320)] (SEQ ID NO:404) and the derived protein sequence for PRO531.

The entire representative nucleotide sequence of UNQ332 (DNA48314-1320) is shown in Figure 162 (SEQ ID NO:404). It is understood that the actual sequence is that within the clone deposited with the ATCC  
25 as DNA48314-1320. Clone UNQ332 (DNA48314-1320) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 171-173 and ending at the stop codon at nucleotide positions 2565-2567 (Figure 162). The predicted polypeptide precursor is 789 amino acids long (Figure 163). The full-length PRO531 protein shown in Figure 163 has an estimated molecular weight of about 87,552 daltons and a pI of about 4.84. Clone UNQ332 (DNA48314-1320) has been deposited with the ATCC on March 26, 1998.

30 Analysis of the amino acid sequence of the full-length PRO531 polypeptide suggests that portions of it possess significant homology to protocadherin 3. Moreover, PRO531 is found in the brain, like other protocadherins, thereby indicating that PRO531 is a novel member of the cadherin superfamily.

Still analyzing the amino acid sequence of SEQ ID NO:405, the cadherin extracellular repeated domain signature is found at about amino acids 122-132, 231-241, 336-346, 439-449 and 549-559 of SEQ ID NO:405.

35 An ATP/GTP-binding site motif A (P-loop) is found at about amino acids 285-292 of SEQ ID NO:405. N-glycosylation sites are found at least at about amino acids 567-570, 786-790, 418-421 and 336-339 of SEQ ID



NO:405. The signal peptide is at about amino acids 1-26, and the transmembrane domain is at about amino acids 685-712 of SEQ ID NO:405.

EXAMPLE 65: Isolation of cDNA Clones Encoding Human PRO534

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43038. Based on the 43048 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO534.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CACAGAGCCAGAAGTGGCGGAATC-3' (SEQ ID NO:411);

reverse PCR primer 5'-CCACATGTTCTCCTGCTCTTGTCCTGG-3' (SEQ ID NO:412).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA43038 sequence which had the following nucleotide sequence:

hybridization probe

5'-CGGTAGTGACTGTACTCTAGTCCTGTTTTACACCCCGTGGTGCCG-3' (SEQ ID NO:413).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO534 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB26).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO534 [herein designated as UNQ335 (DNA48333-1321)] (SEQ ID NO:409) and the derived protein sequence for PRO534.

The entire nucleotide sequence of UNQ335 (DNA48333-1321) is shown in Figure 164 (SEQ ID NO:409). Clone UNQ335 (DNA48333-1321) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 87-89 and ending at the stop codon at nucleotide positions 1167-1169 (Figure 164). The predicted polypeptide precursor is 360 amino acids long (Figure 165). The full-length PRO534 protein shown in Figure 165 has an estimated molecular weight of about 39,885 daltons and a pI of about 4.79. Clone UNQ335 (DNA48333-1321) has been deposited with ATCC on March 26, 1998. It is understood that the deposited clone contains the actual sequence, and that the sequences provided herein are representative based on current sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO534 polypeptide suggests that portions of it possess significant sequence identity with the protein disulfide isomerase, thereby indicating that PRO534 may be a novel disulfide isomerase.

Still analyzing the amino acid sequence of PRO534, the signal peptides is at about amino acids 1-25 of SEQ ID NO:410. The transmembrane domain is at about amino acids 321-340 of SEQ ID NO:410. The disulfide isomerase corresponding region is at amino acids 212-302 of SEQ ID NO:410. The thioredoxin domain is at amino acids 211-227 of SEQ ID NO:410. N-glycosylation sites are at: 165-168, 181-184, 187-190, 194-

197, 206-209, 278-281, and 293-296 of SEQ ID NO:410. The corresponding nucleotides can routinely be determined from the sequences provided herein. PRO534 has a transmembrane domain rather than an ER retention peptide like other protein disulfide isomerases. Additionally, PRO534 may have an intron at the 5 prime end.

#### 5 EXAMPLE 66: Isolation of cDNA Clones Encoding Human PRO697

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43052. Based on this consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO697.

10 A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGCTCGCTGCTGCTGCTC-3' (SEQ ID NO:416);

reverse PCR primer 5'-CCTCACAGGTGCACTGCAAGCTGTC-3' (SEQ ID NO:417).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43052 consensus sequence which had the following nucleotide sequence:

15 hybridization probe

5'-CTCTTCCTCTTTGGCCAGCCCGACTTCTCTACAAGCGCAGAATTGC-3' (SEQ ID NO:418).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO697 gene using the probe oligonucleotide and one of the PCR primers. RNA  
20 for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO697 (herein designated as UNQ361 (DNA50920-1325) (SEQ ID NO:414) and the derived protein sequence for PRO697.

The entire nucleotide sequence of UNQ361 (DNA50920-1325) is shown in Figure 166 (SEQ ID  
25 NO:414). Clone UNQ361 (DNA50920-1325) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 44-46 and ending at the stop codon at nucleotide positions 929-931 (Figure 166). The predicted polypeptide precursor is 295 amino acids long (Figure 167). The full-length PRO697 protein shown in Figure 167 has an estimated molecular weight of about 33,518 daltons and a pI of about 7.74. Clone UNQ361 (DNA50920-1325) was deposited with the ATCC on March 26, 1998. It is understood that the  
30 deposited clone contains the actual sequence, and that the sequences provided herein are representative based on current sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO697 polypeptide suggests that portions of it possess significant sequence identity with sFRPs, thereby indicating that PRO697 may be a novel sFRP family member.

35 Still analyzing the amino acid sequence of PRO697, the signal peptides is at about amino acids 1-20 of SEQ ID NO:415. The cystein rich domain, having identity with the frizzled N-terminus, is at about amino acids

6-153 of SEQ ID NO:415. The corresponding nucleotides can routinely be determined from the sequences provided herein.

**EXAMPLE 67: Isolation of cDNA Clones Encoding Human PRO717**

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42829. Based on the DNA42829 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO717.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGCTTCTCAGCCCTCCTGGAGCAG-3' (SEQ ID NO:421);  
reverse PCR primer 5'-CGGGTCAATAAACCTGGACGCTTGG-3' (SEQ ID NO:422).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA42829 consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-TATGTGGACCGGACCAAGCACTTCACTGAGGCCACCAAGATTG-3' (SEQ ID NO:423).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO717 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue (LIB229).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO717 [herein designated as UNQ385 (DNA50988-1326)] (SEQ ID NO:419) and the derived protein sequence for PRO717.

The entire nucleotide sequence of UNQ385 (DNA50988-1326) is shown in Figure 168 (SEQ ID NO:419). Clone UNQ385 (DNA50988-1326) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1697-1699 (Figure 168). The predicted polypeptide precursor is 560 amino acids long (Figure 169). The full-length PRO717 protein shown in Figure 169 has an estimated molecular weight of about 58,427 daltons and a pI of about 6.86. Clone UNQ385 (DNA50988-1326) has been deposited with the ATCC on April 28, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO717 polypeptide suggests that PRO717 may be a novel 12 transmembrane receptor. The reverse complement strand of DNA50988 has a stretch that matches identically with human regulatory myosin light strand.

Still analyzing the amino acid sequence of SEQ ID NO:420, transmembrane domains are at about amino acids 30-50, 61-79, 98-112, 126-146, 169-182, 201-215, 248-268, 280-300, 318-337, 341-357, 375-387, and 420-441 of SEQ ID NO:420. N-glycosylation sites are at about amino acids 40-43 and 43-46 of SEQ ID

NO:420. A glycosaminoglycan attachment site is at about amino acids 468-471 of SEQ ID NO:420. The corresponding nucleotides can be routinely determined given the sequences provided herein.

EXAMPLE 68: Isolation of cDNA Clones Encoding Human PRO731

A database was used to search expressed sequence tag (EST) databases. The EST database used herein  
5 was the proprietary EST DNA database LIFESEQ™, of Incyte Pharmaceuticals, Palo Alto, CA. Incyte clone 2581326 was herein identified and termed DNA42801. Based on the DNA42801 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO731.

A pair of PCR primers (forward and reverse) were synthesized:

10 forward PCR primer 5'-GTAAGCACATGCCTCCAGAGGTGC-3' (SEQ ID NO:426);  
reverse PCR primer 5'-GTGACGTGGATGCTTGGGATGTTG-3' (SEQ ID NO:427).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA42801 sequence which had the following nucleotide sequence:

hybridization probe  
15 5'-TGGACACCTTCAGTATTGATGCCAAGACAGGCCAGGTCATTCTGCGTCGA-3' (SEQ ID NO:428).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO731 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255). The cDNA  
20 libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, ~~linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel~~ electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280  
25 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO731 [herein designated as UNQ395 (DNA48331-1329)] (SEQ ID NO:424) and the derived protein sequence for PRO731.

The entire nucleotide sequence of UNQ395 (DNA48331-1329) is shown in Figures 170A-B (SEQ ID  
30 NO:424). Clone UNQ395 (DNA48331-1329) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 329-331 and ending at the stop codon at nucleotide positions 3881-3883 (Figures 170A-B). The predicted polypeptide precursor is 1184 amino acids long (Figure 171). The full-length PRO731 protein shown in Figure 171 has an estimated molecular weight of about 129,022 daltons and a pI of about 5.2. Clone UNQ395 (DNA48331-1329) was deposited with the ATCC on March 31, 1998. Regarding  
35 the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO731 polypeptide suggests that portions of it possess significant identity and similarity to members of the protocadherin family, thereby indicating that PRO731 may be a novel protocadherin.

Still analyzing the amino acid sequence of SEQ ID NO:425, the putative signal peptide is at about amino acids 1-13 of SEQ ID NO:425. The transmembrane domain is at amino acids 719-739 of SEQ ID NO:425. The N-glycosylation of SEQ ID NO:425 are as follows: 415-418, 582-586, 659-662, 662-665, and 857-860. The cadherin extracellular repeated domain signatures are at about amino acids (of SEQ ID NO:425): 123-133, 232-242, 340-350, 448-458, and 553-563. The corresponding nucleotides can be routinely determined given the sequences provided herein.

10 EXAMPLE 69: Isolation of cDNA Clones Encoding Human PRO218

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA17411. Two proprietary Genentech EST sequences were employed in the consensus assembly and are shown in Figure 174 and 175. Based on the DNA17411 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO218.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AAGTGGAGCCGGAGCCTTCC-3' (SEQ ID NO:433);

reverse PCR primer 5'-TCGTTGTTTATGCAGTAGTCGG-3' (SEQ ID NO:434).

20 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA17411 sequence which had the following nucleotide sequence:

hybridization probe

5'-ATTGTTTAAAGACTATGAGATACGTCAGTATGTTGTACAGG-3' (SEQ ID NO:435).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO218 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB28).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO218 [herein designated as UNQ192 (DNA30867-1335)] (SEQ ID NO:429) and the derived protein sequence for PRO218.

The entire nucleotide sequence of UNQ192 (DNA30867-1335) is shown in Figure 172 (SEQ ID NO:429). Clone UNQ192 (DNA30867-1335) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 150-152 and ending at the stop codon at nucleotide positions 1515-1517 (Figure 172). The predicted polypeptide precursor is 455 amino acids long (Figure 173). The full-length PRO218 protein shown in Figure 173 has an estimated molecular weight of about 52,917 daltons and a pI of about 9.5. Clone UNQ192 (DNA30867-1335) has been deposited with the ATCC on April 28, 1998. Regarding

the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO218 polypeptide suggests that PRO218 may be a novel transmembrane protein.

Still analyzing the amino acid sequence of SEQ ID NO:430, the putative signal peptide is at about amino acids 1 through 23 of SEQ ID NO:430. Transmembrane domains are potentially at about amino acids 37-55, 81-102, 150-168, 288-311, 338-356, 375-398, and 425-444 of SEQ ID NO:430. N-glycosylation sites are at about amino acids 67, 180, and 243 of SEQ ID NO:430. Eukaryotic cobalamin-binding protein is at about amino acids 151-160 of SEQ ID NO:430. The corresponding nucleotides can be routinely determined given the sequences provided herein.

#### EXAMPLE 70: Isolation of cDNA Clones Encoding Human PRO768

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43448. Based on the DNA43448 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO768.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GGCTGACACCGCAGTGCTCTTCAG-3' (SEQ ID NO:438);

reverse PCR primer 5'-GCTGCTGGGGACTGCAATGTAGCTG-3' (SEQ ID NO:439).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43448 consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-CATCCTCCATGTCTCCCATGAGGTCTCTATTGCTCCACGAAGCATC-3' (SEQ ID NO:440).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO768 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO768 [herein designated as UNQ406 (DNA55737-1345)] (SEQ ID NO:436) and the derived protein sequence for PRO768.

The entire nucleotide sequence of UNQ406 (DNA55737-1345) is shown in Figures 176A-B (SEQ ID NO:436). Clone UNQ406 (DNA55737-1345) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 20-22 and ending at the stop codon at nucleotide positions 3443-3445 (Figures 176A-B). The predicted polypeptide precursor is 1141 amino acids long (Figure 177). The full-length PRO768 protein shown in Figure 177 has an estimated molecular weight of about 124,671 daltons and a pI of about 5.82. Clone UNQ406 (DNA55737-1345) has been deposited with the ATCC on April 6, 1998. Regarding

the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO768 polypeptide suggests that portions of it possess significant sequence identity and similarity with integrin 7.

Still analyzing the amino acid sequence of SEQ ID NO:437, the putative signal peptide is at about amino acids 1-33 of SEQ ID NO:437. The transmembrane domain is at amino acids 1039-1064 of SEQ ID NO:437. N-glycosylation sites are at amino acids: 86-89, 746-749, 949-952, 985-988 and 1005-1008 of SEQ ID NO:437. Integrin alpha chain protein domains are identified at about amino acids: 1064-1071, 384-409, 1041-1071, 317-346, 443-465, 385-407, 215-224, 634-647, 85-99, 322-346, 470-479, 442-466, 379-408 and 1031-1047 of SEQ ID NO:437. The corresponding nucleotides can be routinely determined given the sequences provided herein.

10

#### EXAMPLE 71: Isolation of cDNA Clones Encoding Human PRO771

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43330. Based on the DNA43330 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO771.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CAGCAATATTCAGAAGCGGCAAGGG-3' (SEQ ID NO:443);

reverse PCR primer 5'-CATCATGGTCATCACCACCATCATCATC-3' (SEQ ID NO:444).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43330 consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-GCTTACTACAAGCCAACAGAAATGTCATGGCAGTCTTCACAGTGTGG-3' (SEQ ID NO:445).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO771 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB28).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO771 [herein designated as UNQ409 (DNA49829-1346)] (SEQ ID NO:441) and the derived protein sequence for PRO771.

The entire nucleotide sequence of UNQ409 (DNA49829-1346) is shown in Figure 178 (SEQ ID NO:441). Clone UNQ409 (DNA49829-1346) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 134-136 and ending at the stop codon at nucleotide positions 1442-1444 (Figure 178). The predicted polypeptide precursor is 436 amino acids long (Figure 179). The full-length PRO771 protein shown in Figure 179 has an estimated molecular weight of about 49,429 daltons and a pI of about 4.8. Clone UNQ409 (DNA49829-1346) has been deposited with the ATCC on April 7, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided

herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO771 polypeptide suggests that portions of it possess significant homology to the testican protein, thereby indicating that PRO771 may be a novel testican homologue.

Still analyzing the amino acid sequence of SEQ ID NO:442, the putative signal peptide, leucine zipper pattern, N-myristoylation sites, and thyroglobulin type-1 repeats are also shown in Figure 179. The  
5 corresponding nucleotides can be routinely determined given the sequences provided herein.

EXAMPLE 72: Isolation of cDNA Clones Encoding Human PRO733

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1  
10 above, wherein the consensus sequence obtained is herein designated DNA45600. Based on the DNA45600 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO733.

A pair of PCR primers (forward and reverse) were synthesized:

15 forward PCR primer 5'-CCCAGCAGGGATGGGCGACAAGA-3' (SEQ ID NO:448);

reverse PCR primer 5'-GTCTTCCAGTTTCATATCCAATA-3' (SEQ ID NO:449).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45600 consensus sequence which had the following nucleotide sequence:

hybridization probe

20 5'-CCAGAAGGAGCACGGGGAAGGGCAGCCAGATCTTGTGCGCCCAT-3' (SEQ ID NO:450).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO733 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255).

25 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO733 [herein designated as UNQ411 (DNA52196-1348)] (SEQ ID NO:446) and the derived protein sequence for PRO733.

The entire nucleotide sequence of UNQ411 (DNA52196-1348) is shown in Figures 180A-B (SEQ ID NO:446). Clone UNQ411 (DNA52196-1348) contains a single open reading frame with an apparent translational  
30 initiation site at nucleotide positions 106-108 and ending at the stop codon at nucleotide positions 793-795 (Figures 180A-B). The predicted polypeptide precursor is 229 amino acids long (Figure 181). The full-length PRO733 protein shown in Figure 181 has an estimated molecular weight of about 26,017 daltons and a pI of about 4.73. Clone UNQ411 (DNA52196-1348) has been deposited with the ATCC on April 7, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided  
35 herein are based on known sequencing techniques.



Analysis of the amino acid sequence of the full-length PRO733 polypeptide suggests that portions of it possess significant sequence identity and similarity to the T1/ST2 receptor binding protein precursor and therefore may have a similar function in cell signaling. If it is a cytokine, it may be useful in the treatment of inflammation and cancer.

Still analyzing the amino acid sequence of SEQ ID NO:447, the putative signal peptide, transmembrane domain, N-myristoylation site, and tyrosine kinase site are also shown in Figure 181. The corresponding nucleotides can be routinely determined given the sequences provided herein.

**EXAMPLE 73: Isolation of cDNA Clones Encoding Human PRO162**

An expressed sequence tag (EST) DNA database (Merck/Washington University) was searched and an EST AA397543 was identified which showed homology to human pancreatitis-associated protein. The EST AA397543 clone was purchased and its insert obtained and sequenced and the sequence obtained is shown in Figure 182 (SEQ ID NO:451).

The entire nucleotide sequence of PRO162 is shown in Figure 182 (SEQ ID NO:451). DNA sequencing of the clone gave the full-length DNA sequence for PRO162 [herein designated as UNQ429 (DNA56965-1356)] (SEQ ID NO:451) and the derived protein sequence for PRO162. Clone UNQ429 (DNA56965-1356) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 86-88 and ending at the stop codon at nucleotide positions 611-613 (Figure 182). The predicted polypeptide precursor is 175 amino acids long (Figure 183). The full-length PRO162 protein shown in Figure 183 has an estimated molecular weight of about 19,330 daltons and a pI of about 7.25. Clone UNQ429 (DNA56965-1356) has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO162 polypeptide suggests that portions of it possess significant homology to the human pancreatitis-associated protein, thereby indicating that PRO162 may be a novel pancreatitis-associated protein.

Still analyzing the amino acid sequence of SEQ ID NO:452, the putative signal peptide is at about amino acids 1-26 of SEQ ID NO:452. A C-type lectin domain signature is at about amino acids 146-171 of SEQ ID NO:452. The corresponding nucleotides can be routinely determined given the sequences provided herein.

**EXAMPLE 74: Isolation of cDNA Clones Encoding Human PRO788**

A consensus DNA sequence (designated herein as DNA49308) was assembled relative to other EST sequences using phrap as described in Example 1 above. Based upon an observed homology between the DNA49308 consensus sequence and the Incyte EST clone no. 2777282, the Incyte EST clone no. 2777282 was purchased and its insert obtained and sequenced, which gave the full-length DNA sequence for PRO788 [herein designated as UNQ430 (DNA56405-1357)] (SEQ ID NO:453) and the derived protein sequence for PRO788.

Clone UNQ430 (DNA56405-1357) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 84-86 and ending at the stop codon at nucleotide positions 459-461 (Figure

184). The predicted polypeptide precursor is 125 amino acids long (Figure 185). The full-length PRO788 protein shown in Figure 185 has an estimated molecular weight of about 13,115 daltons and a pI of about 5.90. Clone UNQ430 (DNA56405-1357) has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

- 5 Still analyzing Figure 185, a signal peptide is shown at about amino acids 1-17 of SEQ ID NO:454. An N-glycosylation site is at about amino acids 46-49 of SEQ ID NO:454.

EXAMPLE 75: Isolation of cDNA Clones Encoding Human PRO1008

- 10 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated as DNA49804. An EST proprietary to Genentech was employed in the consensus assembly and is herein designated as DNA16508 (Figure 188; SEQ ID NO:457). Based upon an observed homology between the DNA49804 sequence and Merck EST clone no. AA143670, the Merck EST clone no. AA143670 was purchased and its insert obtained and sequenced. That sequence is shown herein in Figure 186 (SEQ ID NO:455).

- 15 Sequencing gave the full length sequence for PRO1008 [herein designated as UNQ492 (DNA57530-1375)] (SEQ ID NO:455) and the derived protein sequence for PRO1008 were identified.

- The entire nucleotide sequence of UNQ492 (DNA57530-1375) is shown in Figure 186 (SEQ ID NO:455). Clone UNQ492 (DNA57530-1375) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 138-140 and ending at the stop codon at nucleotide positions 936-938 (Figure 186). The predicted polypeptide precursor is 266 amino acids long (Figure 187). The full-length PRO1008 protein shown in Figure 187 has an estimated molecular weight of about 28,672 daltons and a pI of about 8.85. Clone UNQ492 (DNA57530-1375) has been deposited with the ATCC on May 20, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

- 25 Analysis of the amino acid sequence of the full-length PRO1008 polypeptide suggests that portions of it possess significant sequence identity and/or similarity with mdck-1, thereby indicating that PRO1008 may be a novel member of this family and have head inducing activity.

- Still analyzing the amino acid sequence of SEQ ID NO:456, the putative signal peptide is at about amino acids 1-23 of SEQ ID NO:456. The N-glycosylation site is at about amino acids 256-259 of SEQ ID NO:456, and the fungal zn-(2)-cys(6) binuclear cluster domain is at about amino acids 110-126 of SEQ ID NO:456. The corresponding nucleotides of all the amino acids can be routinely determined given the sequences provided herein.

EXAMPLE 76: Isolation of cDNA Clones Encoding Human PRO1012

- 30 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, wherein the consensus sequence is herein designated DNA49313. Based on the DNA49313

consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1012.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-ACTCCCCAGGCTGTTCACACTGCC-3' (SEQ ID NO:460);

5 reverse PCR primer 5'-GATCAGCCAGCCAATACCAGCAGC-3' (SEQ ID NO:461).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA49313 consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-GTGGTGATGATAGAATGCTTTGCCGAATGAAAGGAGTCAACAGCTATCCC-3' (SEQ ID NO:462).

10 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1012 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for  
15 PRO1012 [herein designated as UNQ495 (DNA56439-1376)] (SEQ ID NO:458) and the derived protein sequence for PRO1012.

The entire nucleotide sequence of UNQ495 (DNA56439-1376) is shown in Figures 189A-B (SEQ ID NO:458). Clone UNQ495 (DNA56439-1376) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 404-406 and ending at the stop codon at nucleotide positions 2645-2647  
20 (Figures 189A-B). The predicted polypeptide precursor is 747 amino acids long (Figure 190). The full-length PRO1012 protein shown in Figure 190 has an estimated molecular weight of about 86,127 daltons and a pI of about 7.4. Clone UNQ495 (DNA56439-1376) has been deposited with ATCC on May 14, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

25 Analysis of the amino acid sequence of the full-length PRO1012 polypeptide suggests that portions of it possess sequence identity with disulfide isomerase thereby indicating that PRO1012 may be a novel disulfide isomerase related protein.

Still analyzing the amino acid sequence of SEQ ID NO:459, the cytochrome C family heme-binding site signature is at about amino acids 158-163 of SEQ ID NO:459. The Nt-DNAJ domain signature is at about amino  
30 acids 77-96 of SEQ ID NO:459. An N-glycosylation site is at about amino acids 484-487 of SEQ ID NO:459.

The ER targeting sequence is at about amino acids 744-747 of SEQ ID NO:459. It is understood that the polypeptide and nucleic acids disclosed can be routinely formed with or without, these portions as desired, in alternative embodiments. For example, it may be desirable to produce PRO1012 without the ER targeting sequence. The corresponding nucleotides can be routinely determined given the sequences provided herein.

35

**EXAMPLE 77: Isolation of cDNA Clones Encoding Human PRO1014**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA49811. Based upon an observed homology between the DNA49811 sequence and Incyte EST clone no. 2612207, Incyte EST clone no. 2612207 was purchased and its insert was obtained and sequenced, wherein the sequence obtained is shown in Figure 191 (SEQ ID NO:463).

DNA sequencing gave the full-length DNA sequence for PRO1014 [herein designated as UNQ497 (DNA56409-1377)] (SEQ ID NO:463) and the derived protein sequence for PRO1014.

The entire nucleotide sequence of UNQ497 (DNA56409-1377) is shown in Figure 191 (SEQ ID NO:463). Clone UNQ497 (DNA56409-1377) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 66-68 and ending at the stop codon at nucleotide positions 966-968 (Figure 191). The predicted polypeptide precursor is 300 amino acids long (Figure 192). The full-length PRO1014 protein shown in Figure 192 has an estimated molecular weight of about 33,655 daltons and a pI of about 9.31. Clone UNQ497 (DNA56409-1377) has been deposited with the ATCC on May 20, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1014 polypeptide suggests that portions of it possess sequence identity with reductase, thereby indicating that PRO1014 may be a novel member of the reductase family.

Still analyzing the amino acid sequence of SEQ ID NO:464, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:464. The cAMP and cGMP dependent protein kinase phosphorylation sites are at about amino acids 30-33 and 58-61 of SEQ ID NO:464. Short chain alcohol dehydrogenase family proteins are at about amino acids 165-202, 37-49, 112-122 and 210-219 of SEQ ID NO:464. The corresponding nucleotides of these domains and any other amino acids provided herein can be routinely determined given the sequences provided herein.

**EXAMPLE 78: Isolation of cDNA Clones Encoding Human PRO1017**

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, wherein that consensus DNA sequence is herein designated DNA53235. Based upon an observed homology between the DNA53235 consensus sequence and the Merck EST clone no. AA243086, the Merck EST clone no. AA243086 was purchased and its insert obtained and sequenced, wherein the sequence obtained is shown in Figure 193 (SEQ ID NO:465). DNA sequencing gave the full-length DNA sequence for PRO1017 [herein designated as UNQ500 (DNA56112-1379)] (SEQ ID NO:465) and the derived protein sequence for PRO1017.

The entire nucleotide sequence of UNQ500 (DNA56112-1379) is shown in Figure 193 (SEQ ID NO:465). Clone UNQ500 (DNA56112-1379) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 128-130 and ending at the stop codon at nucleotide positions 1370-1372

(Figure 193). The predicted polypeptide precursor is 414 amino acids long (Figure 194). The full-length PRO1017 protein shown in Figure 194 has an estimated molecular weight of about 48,414 daltons and a pI of about 9.54. Clone UNQ500 (DNA56112-1379) has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

5        Analysis of the amino acid sequence of the full-length PRO1017 polypeptide suggests that portions of it possess sequence identity with HNK-1 sulfotransferase, thereby indicating that PRO1017 may be a novel sulfotransferase.

      Still analyzing the amino acid sequence of SEQ ID NO:466, the putative signal peptide is at about amino acids 1-31 of SEQ ID NO:466. N-glycosylation sites are at about amino acids 134-137, 209-212, 280-283 and  
10    370-273 of SEQ ID NO:466. The TNFR/NGFR family cystein-rich region protein is at about amino acids 329-332 of SEQ ID NO:466. The corresponding nucleotides can be routinely determined given the sequences provided herein. The protein can be secreted.

EXAMPLE 79: Isolation of cDNA Clones Encoding Human PRO474

15        A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA49818. Based upon an observed homology between the DNA49818 consensus sequence and the Merck EST clone no. H77889, the Merck EST clone no. H77889 was purchased and its insert obtained and sequenced, wherein the sequence obtained is herein shown in Figure 195 (SEQ ID NO:467). DNA sequencing gave the full-length DNA sequence  
20    for PRO474 [herein designated as UNQ502 (DNA56045-1380)] (SEQ ID NO:467) and the derived protein sequence for PRO474.

      The entire nucleotide sequence of UNQ502 (DNA56045-1380) is shown in Figure 195 (SEQ ID NO:467). Clone UNQ502 (DNA56045-1380) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 106-108 and ending at the stop codon at nucleotide positions 916-918  
25    (Figure 195). The predicted polypeptide precursor is 270 amino acids long (Figure 196). The full-length PRO474 protein shown in Figure 196 has an estimated molecular weight of about 28,317 daltons and a pI of about 6.0. Clone UNQ502 (DNA56045-1380) has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

30        Still analyzing the amino acid sequence of SEQ ID NO:468, an N-glycosylation site is at about amino acids 138-141 of SEQ ID NO:468. Short-chain alcohol dehydrogenase family proteins are at about amino acids 10-22, 81-91, 134-171 and 176-185 of SEQ ID NO:468. The corresponding nucleotides can be routinely determined given the sequences provided herein.

35    EXAMPLE 80: Isolation of cDNA Clones Encoding Human PRO1031

      An initial consensus DNA sequence was assembled relative to other EST sequences using phrap as

described in Example 1 above, wherein the consensus sequence obtained is herein designated as DNA47332. Based upon an observed homology between the DNA47332 sequence and the Merck EST clone no. W74558, Merck EST clone no. W74558 was purchased and its insert obtained and sequenced, wherein the sequence obtained is shown in Figure 197 (SEQ ID NO:469). DNA sequencing gave the full-length DNA sequence for PRO1031 [herein designated as UNQ516 (DNA59294-1381)] (SEQ ID NO:469) and the derived protein sequence for PRO1031.

The entire nucleotide sequence of UNQ516 (DNA59294-1381) is shown in Figure 197 (SEQ ID NO:469). Clone UNQ516 (DNA59294-1381) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon at nucleotide positions 582-584 (Figure 197). The predicted polypeptide precursor is 180 amino acids long (Figure 198). The full-length PRO1031 protein shown in Figure 198 has an estimated molecular weight of about 20,437 daltons and a pI of about 9.58. Clone UNQ516 (DNA59294-1381) has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1031 polypeptide suggests that it is a novel cytokine.

Still analyzing the amino acid sequence of SEQ ID NO:470, the putative signal peptide is at about amino acids 1-20 of SEQ ID NO:470. An N-glycosylation site is at about amino acids 75-78 of SEQ ID NO:470. A region having sequence identity with IL-17 is at about amino acids 96-180. The corresponding nucleotides can be routinely determined given the sequences provided herein.

#### EXAMPLE 81: Isolation of cDNA Clones Encoding Human PRO938

A consensus DNA sequence was assembled relative to other EST sequences using the procedure described in Example 1 above, wherein that consensus sequence is herein designated DNA49798. Based on the DNA49798 DNA consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO938.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GTCCAGCCCATGACCGCCTCCAAC-3' (SEQ ID NO:473)

reverse PCR primer 5'-CTCTCCTCATCCACACCAGCAGCC-3' (SEQ ID NO:474)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA49798 sequence which had the following nucleotide sequence:

hybridization probe

5'-GTGGATGCTGAAATTTTACGCCCCATGGTGTCCATCCTGCCAGC-3' (SEQ ID NO:475)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO938 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO938 [herein designated as UNQ475 (DNA56433-1406)] (SEQ ID NO:471) and the derived protein sequence for PRO938.

The entire nucleotide sequence of UNQ475 (DNA56433-1406) is shown in Figure 199 (SEQ ID NO:471). Clone UNQ475 (DNA56433-1406) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 134-136 and ending at the stop codon at nucleotide positions 1181-1183 (Figure 199). The predicted polypeptide precursor is 349 amino acids long (Figure 200). The full-length PRO938 protein shown in Figure 200 has an estimated molecular weight of about 38,952 daltons and a pI of about 4.34. Analysis of the full-length PRO938 sequence shown in Figure 200 (SEQ ID NO:472) evidences the presence of the following features: a signal peptide from amino 1 to about amino acid 22, a transmembrane domain from about amino acid 191 to about amino acid 211, a potential N-glycosylation site from about amino acid 46 to about amino acid 49, a region homologous to disulfide isomerase from about amino acid 56 to about amino acid 72, and a region having sequence identity with flavodoxin proteins from about amino acid 173 to about amino acid 187.

Clone UNQ475 (DNA56433-1406) has been deposited with ATCC on May 12, 1998, and is assigned ATCC Accession No. 209857.

Analysis of the amino acid sequence of the full-length PRO938 polypeptide suggests that it possesses significant sequence similarity to protein disulfide isomerase, thereby indicating that PRO938 may be a novel protein disulfide isomerase. An analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO938 amino acid sequence and the following Dayhoff sequences, P\_W03626, P\_W03627, P\_R70491, GARP\_PLAFF, XLU85970\_1, ACADISPROA\_1, IE68\_HSVSA, KSU52064\_1, U93872\_83, E\_R57866.

#### EXAMPLE 82: Isolation of cDNA Clones Encoding Human PRO1082

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, wherein the consensus sequence is herein designated DNA38097. Based on this consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1082.

A set of PCR primers (two forward and one reverse) were synthesized:

forward primer 1 5'-GTCCACAGACAGTCATCTCAGGAGCAG-3' (SEQ ID NO:478);

forward primer 2 5'-ACAAGTGTCTTCCCAACCTG-3' (SEQ ID NO:479);

reverse primer 1 5'-ATCCTCCAGAGCCATGGTACCTC-3' (SEQ ID NO:480).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA38097 consensus sequence which had the following nucleotide sequence:

hybridization probe

5'-CCAAGGATAGCTGTTGTTTCAGAGAAAGGATCGTGTGCTGCATCTCCTCCT-3' (SEQ ID NO:481).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primers identified above. A positive library was then used to isolate clones encoding the PRO1082 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1082 [herein designated as UNQ539 (DNA53912-1457)] (SEQ ID NO:476) and the derived protein sequence for PRO1082.

The entire nucleotide sequence of UNQ539 (DNA53912-1457) is shown in Figure 201 (SEQ ID NO:476). Clone UNQ539 (DNA53912-1457) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 160-162 and ending at the stop codon at nucleotide positions 763-765 (Figure 201). The predicted polypeptide precursor is 201 amino acids long (Figure 202). The full-length PRO1082 protein shown in Figure 202 has an estimated molecular weight of about 22,563 daltons and a pI of about 4.87. Clone UNQ539 (DNA53912-1457) has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:477, the transmembrane domain is at about amino acids 45-65 of SEQ ID NO:477. A cAMP- and cGMP-dependent protein kinase phosphorylation site is at about amino acids 197-200 of SEQ ID NO:477. N-myristoylation sites are at about amino acids 35-40 and 151-156 of SEQ ID NO:477. The regions which share sequence identity with the LDL receptor are at about amino acids 34-67 and 70-200 of SEQ ID NO:477. The corresponding nucleotides of these amino acid regions and others can be routinely determined given the sequences provided herein.

#### EXAMPLE 83: Isolation of cDNA Clones Encoding Human PRO1083

A cDNA sequence was identified using the amylase screening technique described in Example 2 above, wherein that cDNA sequence is designated herein as DNA24256 (Figure 205; SEQ ID NO:484). That cDNA sequence was then compared and aligned with other known EST sequences as described in Example 1 above to obtain a consensus DNA sequence which is designated herein as DNA43422. Based on the DNA 43422 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1083.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GGCATTGGAGCAGTGCTGGGTG-3' (SEQ ID NO:485);

reverse PCR primer 5'-TGGAGGCCTAGATGCGGCTGGACG-3' (SEQ ID NO:486).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1083 gene using the reverse PCR primer. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).



DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1083 [herein designated as UNQ540 (DNA50921-1458)] (SEQ ID NO:482) and the derived protein sequence for PRO1083.

The entire nucleotide sequence of UNQ540 (DNA50921-1458) is shown in Figure 203 (SEQ ID NO:482). Clone UNQ540 (DNA50921-1458) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 214-216 and ending at the stop codon at nucleotide positions 2293-2295 (Figure 203). The predicted polypeptide precursor is 693 amino acids long (Figure 204). The full-length PRO1083 protein shown in Figure 204 has an estimated molecular weight of about 77,738 daltons and a pI of about 8.87. Clone UNQ540 (DNA50921-1458) has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:483, the putative signal peptide is at about amino acids 1-25 of SEQ ID NO:483. The transmembrane domains are at about amino acids 382-398, 402-420, 445-468, 473-491, 519-537, 568-590 and 634-657 of SEQ ID NO:483. A microbodies C-terminal targeting signal is at about amino acids 691-693 of SEQ ID NO:483. cAMP- and cGMP-dependent protein kinase phosphorylation sites are at about amino acids 198-201 and 370-373 of SEQ ID NO:483. N-glycosylation sites are at about amino acids 39-42, 148-151, 171-174, 234-237, 303-306, 324-227 and 341-344 of SEQ ID NO:483. A G-protein coupled receptor family domain is at about amino acids 475-504 of SEQ ID NO:483. The corresponding nucleotides can be routinely determined given the sequences provided herein.

#### 20 EXAMPLE 84: Isolation of cDNA Clones Encoding Human PRO200

Probes based on an expressed sequence tag (EST) identified from the Incyte Pharmaceuticals database due to homology with VEGF were used to screen a cDNA library derived from the human glioma cell line C6. In particular, Incyte Clone "INC1302516" was used to generate the following four probes:

- (SEQ ID NO:489) ACTTCTCAGTGTCCATAAGGG;  
 25 (SEQ ID NO:490) GAACTAAAGAGAACCGATACCATTCTGGCCAGGTTGTC;  
 (SEQ ID NO:491) CACCACAGCGTTTAACCAGG; and  
 (SEQ ID NO:492) ACAACAGGCACAGTTCCAC.

Nine positives were identified and characterized. Three clones contained the full coding region and were identical in sequence. Partial clones were also identified from a fetal lung library and were identical with the glioma-derived sequence with the exception of one nucleotide change which did not alter the encoded amino acid.

#### EXAMPLE 85: Expression Constructs for PRO200

For mammalian protein expression, the entire open reading frame (ORF) was cloned into a CMV-based expression vector. An epitope-tag (FLAG, Kodak) and Histidine-tag (His8) were inserted between the ORF and stop codon. VEGF-E-His8 and VEGF-E-FLAG were transfected into human embryonic kidney 293 cells by

SuperFect (Qiagen) and pulse-labeled for 3 hours with [<sup>35</sup>S]methionine and [<sup>35</sup>C]cysteine. Both epitope-tagged proteins co-migrate when 20 microliters of 15-fold concentrated serum-free conditioned medium were electrophoresed on a polyacrylamide gel (Novex) in sodium dodecyl sulfate sample buffer (SDS-PAGE). The VEGF-E-IgG expression plasmid was constructed by cloning the ORF in front of the human Fc (IgG) sequence.

The VEGF-E-IgG plasmid was co-transfected with Baculogold Baculovirus DNA (Pharmingen) using Lipofectin (GibcoBRL) into 10<sup>5</sup> Sf9 cells grown in Hink's TNM-FH medium (JRH Biosciences) supplemented with 10% fetal bovine serum. Cells were incubated for 5 days at 28°C. The supernatant was harvested and subsequently used for the first viral amplification by infecting Sf9 cells at an approximate multiplicity of infection (MOI) of 10. Cells were incubated for 3 days, then supernatant harvested, and expression of the recombinant plasmid determined by binding of 1 ml of supernatant to 30 µl of Protein-A Sepharose CL-4B beads (Pharmacia) followed by subsequent SDS-PAGE analysis. The first amplification supernatant was used to infect a 500 ml spinner culture of Sf9 cells grown in ESF-921 medium (Expression Systems LLC) at an approximate MOI of 0.1. Cells were treated as above, except harvested supernatant was sterile filtered. Specific protein was purified by binding to Protein-A Sepharose 4 Fast Flow (Pharmacia) column.

15 Example 86: Northern Blot Analyses for PRO200

Blots of human poly(A)+ RNA from multiple adult and fetal tissues and tumor cell lines were obtained from Clontech (Palo Alto, CA). Hybridization was carried out using <sup>32</sup>P-labeled probes containing the entire coding region and washed in 0.1 x SSC, 0.1% SDS at 63°C.

VEGF-E mRNA was detectable in fetal lung, kidney, brain, liver and adult heart, placenta, liver, skeletal muscle, kidney, and pancreas. VEGF-E mRNA was also found in A549 lung adenocarcinoma and HeLa cervical adenocarcinoma cell lines.

Example 87: In Situ Hybridization of Human Fetal Tissue Sections for PRO200

Formalin-fixed, paraffin-embedded human fetal brain, liver, lower limb, small intestine, thyroid, lymph node, thymus, stomach, trachea, skin, spleen, spinal cord, adrenal, placenta, cord, and adult liver, pancreas, lung, spleen, lymph node, adrenal, heart, aorta, and skin were sectioned, deparaffinized, deproteinized in proteinase K (20 µg/ml) for 15 minutes at 37°C, and further processed for in situ hybridization as described by Lu LH and Gillett NA (Cell Vision 1:169-176, 1994). A [<sup>33</sup>-P]UTP-labeled antisense riboprobe was generated from a PCR product of 980 bp (primers GGCGGAATCCAACCTGAGTAG and GCGGCTATCCTCCTGTGCTC, SEQ ID NOS: 493 and 494, respectively). The slides were dipped in Kodak NTB2 nuclear track emulsion and exposed for 4 weeks.

VEGF-E mRNA expression included localization at the growth plate region and embracing fetal myocytes.

Example 88: Myocyte Hypertrophy Assay for PRO200

Myocytes from neonatal Harlan Sprague Dawley rat heart ventricle (23 days gestation) were plated in duplicate at 75000 cells/ml in a 96-well plate. Cells were treated for 48h with 2000, 200, 20, or 2 ng/ml VEGF-E-IgG. Myocytes were stained with crystal violet to visualize morphology and scored on a scale of 3 to 7, 3 being nonstimulated and 7 being full-blown hypertrophy.

5        2000 ng/ ml and 200 ng/ ml VEGF-E caused hypertrophy, scored as a 5.

Example 89: Cell Proliferation Assay for PRO200

Mouse embryonic fibroblast C3H10T1/2 cells (ATCC) were grown in 50:50 Ham's F-12: low glucose DMEM medium containing 10% fetal calf serum (FCS). Cells were plated in duplicate in a 24-well plate at 10        1000, 2000, and 4000 cells/well. After 48 hours, cells were switched to medium containing 2% FCS and were incubated for 72 hours with 200, 800, or 2000 ng/ml VEGF-E or no growth factor added.

Approximately 1.5 fold greater number of cells were measured in the presence of 200 ng/ml VEGF-E as in its absence, at all three cell densities.

15        Example 90: Endothelial Cell Survival Assay for PRO200

Human umbilical vein endothelial cells (HUVEC, Cell Systems) were maintained in Complete Media (Cell Systems) and plated in triplicate in serum-free medium (Basic Media from Cell Systems containing 0.1% BSA) at 20,000 cells/well of a 48-well plate. Cells were incubated for 5 days with 200 or 400 ng/ml VEGF-E-IgG, 100 ng/ml VEGF, 20 ng/ml basic FGF, or no addition.

20        Survival was 2-3 times greater with VEGF-E as compared to lack of growth factor addition. VEGF and basic FGF were included as positive controls.

EXAMPLE 91: Isolation of cDNA Clones Encoding Human PRO285

A proprietary expressed sequence tag (EST) DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST (#2243209) was identified which showed homology to the *Drosophila* Toll protein.

Based on the EST, a pair of PCR primers (forward and reverse):

TAAAGACCCAGCTGTGACCG (SEQ ID NO:499)

ATCCATGAGCCTCTGATGGG (SEQ ID NO: 500), and

30        a probe:

ATTTATGTCTCGAGGAAAGGGACTGGTTACCAGGGCAGCCAGTTC (SEQ ID NO: 501)

were synthesized.

mRNA for construction of the cDNA libraries was isolated from human placenta tissue. The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available 35        reagents such as those from Invitrogen, San Diego, CA (Fast Track 2). The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately

by gel electrophoresis, and cloned in a defined orientation into the cloning vector pCR2.1 (Invitrogen, Inc.) using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). The double stranded cDNA was sized to greater than 1000 bp and the cDNA was cloned into BamHI/NotI cleaved vector. pCR2.1 is a commercially available plasmid, designed for easy cloning of PCR fragments, that carries AmpR and KanR genes for selection, and LacZ gene for blue-white selection.

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO285 gene using the probe oligonucleotide and one of the PCR primers.

A cDNA clone was sequenced in entirety. The entire nucleotide sequence of DNA40021-1154 (encoding PRO285) is shown in Figure 208 (SEQ ID NO:495). Clone DNA40021-1154 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 (Figure 208). The predicted polypeptide precursor is 1049 amino acids long, including a putative signal peptide at amino acid positions 1-29, a putative transmembrane domain between amino acid positions 837-860, and a leucine zipper pattern at amino acid positions 132-153 and 704-725, respectively. It is noted that the indicated boundaries are approximate, and the actual limits of the indicated regions might differ by a few amino acids. Clone DNA40021-1154 has been deposited with ATCC (designation: DNA40021-1154) and is assigned ATCC deposit no.209389.

Based on a BLAST and FastA sequence alignment analysis (using the ALIGN computer program) of the full-length sequence is a human analogue of the *Drosophila* Toll protein, and is homologous to the following human Toll proteins: Toll1 (DNAX# HSU88540-1, which is identical with the random sequenced full-length cDNA #HUMRSC786-1); Toll2 (DNAX# HSU88878-1); Toll3 (DNAX# HSU88879-1); and Toll4 (DNAX# HSU88880-1).

#### EXAMPLE 92: Isolation of cDNA Clones Encoding Human PRO286

A proprietary expressed sequence tag (EST) DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST (#694401) was identified which showed homology to the *Drosophila* Toll protein.

Based on the EST, a pair of PCR primers (forward and reverse):

GCCGAGACAAAAACGTTCTCC (SEQ ID NO:502)

CATCCATGTTCTCATCCATTAGCC (SEQ ID NO: 503), and

a probe:

TCGACAACCTCATGCAGAGCATCAACCAAAGCAAGAAAACAGTATT (SEQ ID NO: 504)

were synthesized.

mRNA for construction of the cDNA libraries was isolated from human placenta tissue. This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an SfiI restriction enzyme site preceding the XhoI/NotI cDNA cloning sites. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased

adaptors, cleaved with NotI, sized to greater than 1000 bp appropriately by gel electrophoresis, and cloned in a defined orientation into XhoI/NotI-cleaved pRK5D.

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO286 gene using the probe oligonucleotide identified above and one of the PCR primers.

A cDNA clone was sequenced in entirety. The entire nucleotide sequence of DNA42663-1154 (encoding PRO286) is shown in Figures 210A-B (SEQ ID NO:497). Clone DNA42663-1154 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 57-59 (Figure 211). The predicted polypeptide precursor is 1041 amino acids long, including a putative signal peptide at amino acid positions 1-26, a potential transmembrane domain at amino acid positions 826-848, and leucine zipper patterns at amino acids 130-151, 206-227, 662-684, 669-690 and 693-614, respectively. It is noted that the indicated boundaries are approximate, and the actual limits of the indicated regions might differ by a few amino acids. Clone DNA42663-1154 has been deposited with ATCC (designation: DNA42663-1154) and is assigned ATCC deposit no. 209386.

Based on a BLAST and FastA sequence alignment analysis (using the ALIGN computer program) of the full-length sequence of PRO286, it is a human analogue of the *Drosophila* Toll protein, and is homologous to the following human Toll proteins: Toll1 (DNAX# HSU88540-1, which is identical with the random sequenced full-length cDNA #HUMRSC786-1); Toll2 (DNAX# HSU88878-1); Toll3 (DNAX# HSU88879-1); and Toll4 (DNAX# HSU88880-1).

#### Example 93: NF- $\kappa$ B Assay for PRO285 and PRO286

As the Toll proteins signal through the NF- $\kappa$ B pathway, their biological activity can be tested in an NF- $\kappa$ B assay. In this assay Jurkat cells are transiently transfected using Lipofectamine reagent (Gibco BRL) according to the manufacturer's instructions. 1  $\mu$ g pB2XLuc plasmid, containing NF- $\kappa$ B-driven luciferase gene, is cotransfected with 1  $\mu$ g pSR $\alpha$ N expression vector with or without the insert encoding PRO285 or PRO286. For a positive control, cells are treated with PMA (phorbol myristyl acetate; 20 ng/ml) and PHA (phytohaemagglutinin, 2  $\mu$ g/ml) for three to four hours. Cells are lysed 2 or 3 days later for measurement of luciferase activity using reagents from Promega.

#### EXAMPLE 94: Isolation of cDNA Clones Encoding Human PRO213-1, PRO1330 and PRO1449

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA28735. Based on the DNA28735 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO213-1, PRO1330 and/or PRO1449. A pair of PCR primers (forward and reverse) were synthesized:  
forward PCR primer 5'-TGGAGCAGCAATATGCCAGCC-3' (SEQ ID NO:511)

reverse PCR primer 5'-TTTCCACTCCTGTCGGGTTGG-3' (SEQ ID NO:512)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA28735 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGTGACACTTGCCAGTCAGATGTGGATGAATGCAGTGCTAGGAGGG-3' (SEQ ID NO:513)

5 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO213-1, PRO1330 and/or PRO1449 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence encoding  
10 PRO213-1, PRO1330 and/or PRO1449 [DNA30943-1-1163-1 (SEQ ID NO:505), DNA64907-1163-1 (SEQ ID NO:507) and DNA64908-1163-1 (SEQ ID NO:509), respectively].

The entire nucleotide sequences corresponding to DNA30943-1-1163-1 (SEQ ID NO:505), DNA64907-1163-1 (SEQ ID NO:507) and DNA64908-1163-1 (SEQ ID NO:509), respectively. DNA30943-1163, DNA64907-1163-1 and DNA64908-1163-1 contain a single open reading frame with an apparent translational  
15 initiation site at nucleotide positions 336-338, 488-490 and 326-328, respectively, and ending at the stop codon at nucleotide positions 1221-1223, 1307-1309 and 1145-1147, respectively (Figures 212, 214 and 216). The predicted polypeptide precursor is 295, 273 and 273 amino acids long, respectively (Figures 213, 215 and 217). DNA30943-1-1163-1, DNA64907-1163-1 and DNA64908-1163-1 have been deposited with ATCC and are assigned ATCC deposit no. 209791, 203242 and 203243, respectively.

20 Analysis of the amino acid sequence of the full-length PRO213-1 polypeptide suggests that a portion of it possess significant homology to the human growth arrest-specific gene 6 protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO213 amino acid sequence and the following Dayhoff sequences, HSMHC3W5A\_6 and B48089.

Additional analysis of the amino acid sequence of the full-length PRO1330 and PRO1449 polypeptide  
25 indicates significant identity with notch4. More specifically, an analysis of the Dayhoff database (version 35.130 SwissProt 35) evidenced significant identity between PRO1330 and the following Dayhoff sequences, D86566\_1 and NEL\_HUMAN.

#### EXAMPLE 95: Isolation of cDNA Clones Encoding Human PRO298

30 A cDNA isolated in the amylase screen described in Example 2 above is herein designated DNA26832 (Figure 220; SEQ ID NO:516). The sequence of DNA26832 was then used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266: 469-480 [1996]). Those comparisons  
35 resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington,

Seattle, Washington; <http://bozeman.mbt.washington.edu/phrap.docs/phrap.html>).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. A consensus sequence was determined, which was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended assembly sequence was designated DNA35861. Based on the DNA35861 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence of PRO298. Forward and reverse primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequence is typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) and a hybridization probe were synthesized:

forward PCR primer 1 CAACGTGATTTC AAAGCTGGGCTC (SEQ ID NO:517)

forward PCR primer 2 GCCTCGTATCAAGAATTTCC (SEQ ID NO:518)

forward PCR primer 3 AGTGGAAGTCGACCTCCC (SEQ ID NO:519)

reverse PCR primer 1 CTCACCTGAAATCTCTCATAGCCC (SEQ ID NO:520)

hybridization probe 1 CGAAAACCCATTTTGGGAGCAGGAATTCCAATCATGTCTGTGATGGTGG (SEQ ID NO:521)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO298 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO298 (herein designated UNQ261 [DNA39975-1210]) (SEQ ID NO:514), and the derived protein sequence for PRO298 (SEQ ID NO:515).

The entire nucleotide sequence of UNQ261 (DNA39975-1210) is shown in Figure 218 (SEQ ID NO:514). Clone DNA39975-1210 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 375-377. The predicted polypeptide precursor is 364 amino acids long. The protein contains four putative transmembrane domains between amino acid positions 36-55 (type II TM), 65-84, 188-

208, and 229-245, respectively. A putative N-linked glycosylation site starts at amino acid position 253. In addition, the following features have been identified in the protein sequence: cAMP- and cGMP-dependent protein kinase phosphorylation site, starting at position 8; N-myristoylation sites starting a position 173 and 262, respectively; and a ZP domain between amino acid positions 45-60. Clone DNA39975-1210 has been deposited with ATCC (April 21, 1998) and is assigned ATCC deposit no.209783.

5

**EXAMPLE 96: Isolation of cDNA Clones Encoding Human PRO337**

A cDNA sequence identified in the amylase screen described in Example 2 above is herein designated DNA42301 (Figure 223, SEQ ID NO:524). The DNA42301 sequence was then compared to other EST sequences using phrap as described in Example 1 above and a consensus sequence designated herein as DNA28761 was identified. Based on this consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence. In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO337 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain.

A cDNA clone was sequenced in its entirety. The full length nucleotide sequence of DNA43316-1237 is shown in Figure 221 (SEQ ID NO:522). Clone DNA43316-1237 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 134-136 (Figure 221; SEQ ID NO:522). The predicted polypeptide precursor is 344 amino acids long. Clone DNA43316-1237 has been deposited with ATCC and is assigned ATCC deposit no. 209487

Based on a BLAST-2 and FastA sequence alignment analysis of the full-length sequence, PRO337 shows amino acid sequence identity to rat neurotrophin (97%).

**EXAMPLE 97: Isolation of cDNA Clones Encoding Human PRO403**

**25 Introduction:**

Human thrombopoietin (THPO) is a glycosylated hormone of 352 amino acids consisting of two domains. The N-terminal domain, sharing 50% similarity to erythropoietin, is responsible for the biological activity. The C-terminal region is required for secretion. The gene for thrombopoietin (THPO) maps to human chromosome 3q27-q28 where the six exons of this gene span 7 kilobase base pairs of genomic DNA (Chang et al., Genomics 26: 636-7 (1995); Foster et al., Proc. Natl. Acad. Sci. USA 91: 13023-7 (1994); Gurney et al., Blood 85: 981-988 (1995). In order to determine whether there were any genes encoding THPO homologues located in close proximity to THPO, genomic DNA fragments from this region were identified and sequenced. Three P1 clones and one PAC clones (Genome Systems Inc., St. Louis, MO; cat. Nos. P1-2535 and PAC-6539) encompassing the THPO locus were isolated and a 140 kb region was sequenced using the ordered shotgun strategy (Chen et al., Genomics 17: 651-656 (1993)), coupled with a PCR-based gap filling approach. Analysis reveals that the region is gene-rich with four additional genes located very close to THPO: tumor necrosis factor-



receptor type 1 associated protein 2 (TRAP2) and elongation initiation factor gamma (eIF4), chloride channel 2 (CLCN2) and RNA polymerase II subunit hRPB17. While no THPO homolog was found in the region, four novel genes have been predicted by computer-assisted gene detection (GRAIL)(Xu et al., Gen. Engin. 16: 241-253 (1994), the presence of CpG islands (Cross, S. and Bird, A., Curr. Opin. Genet. & Devel. 5: 109-314 (1995), and homology to known genes (as detected by WU-BLAST2.0)(Altschul and Gish, Methods Enzymol. 5 266: 460-480 (1996) (<http://blast.wustl.edu/blast/README.html>).

#### Procedures:

##### P1 and PAC clones:

The initial human P1 clone was isolated from a genomic P1 library (Genome Systems Inc., St. Louis, MO; cat. no.: P1-2535) screened with PCR primers designed from the THPO genomic sequence (A.L. Gurney, et al., Blood 85: 981-88 (1995). PCR primers were designed from the end sequences derived from this P1 clone were then used to screen P1 and PAC libraries (Genome Systems, Cat. Nos.: P1-2535 & PAC-6539) to identify overlapping clones (PAC1, p1.t, and P1.u). The 3'-end sequence from PAC.z was used to define the primers used for the screening of a human BAC library (Genome Systems Inc., St. Louis, MO; Cat. No.: BDTW-4533A).

##### Ordered Shotgun Strategy:

The Ordered Shotgun Strategy (OSS) (Chen et al., Genomics 17: 651-656 (1993)) involves the mapping and sequencing of large genomic DNA clones with a hierarchical approach. The P1 or PAC clone was sonicated and the fragments subcloned into lambda vector ( $\lambda$ BlueStar) (Novagen, Inc., Madison, WI; cat. no. 69242-3). The lambda subclone inserts were isolated by long-range PCR (Barnes, W. Proc. Natl. Acad. Sci. USA 91: 2216-2220 (1994) and the ends sequenced. The lambda-end sequences were overlapped to create a partial map of the original clone. Those lambda clones with overlapping end-sequences were identified, the insets subcloned into a plasmid vector (pUC18 or pUC19, Hoefer Pharmacia Biotech, Inc., San Francisco, CA, Cat. Nos. 27-4949-01 and 27-4951-01) and the ends of the plasmid subclones were sequenced and assembled to generate a contiguous sequence. This directed sequencing strategy minimizes the redundancy required while allowing one 25 to scan for and concentrate on interesting regions.

In order to define better the THPO locus and to search for other genes related to the hematopoietin family, five genomic clones were isolated from this region by PCR screening of human P1 and PAC libraries (Genome System, Inc., Cat. Nos.: P1-2535 and PAC-6539).

The sizes of the genomic fragments are as follows: P1.t is 40 kb; P1.g is 70 kb; P1.u is 70 kb; PAC.z is 200 kb; and BAC.1 is 80 kb. Approximately 75% (140 kb) of the 190 kb genomic DNA region was sequenced by the Ordered Shotgun Strategy (OSS) (Chen et al., Genomics 17: 651-56 (1993), and assembled into contigs using AutoAssemblerTM (Applied Biosystems, Perkin Elmer, Foster City, CA, cat. no. 903227). The preliminary order of these contigs was determined by manual analysis. There were 47 contigs the 140 kb region. A PCR-based approach to ordering the contigs and filling in the gaps was employed. The following summarizes the 35 number and sizes of the gaps. The 50 kb of sequence unique to BAC.1 was sequenced by a total shotgun approach with a ten-fold redundancy.

<u>Size of gap</u>	<u>number</u>
<50 bp	13
50-150 bp	7
150-300 bp	7
300-1000 bp	10
5 1000-5000 bp	7
> 5000 bp	2 ((15,000 bp)

#### DNA sequencing:

ABI DYE-primer<sup>TM</sup> chemistry (PE Applied Biosystems, Foster City, CA; Cat. No.: 402112) was used to end-sequence the lambda and plasmid subclones. ABI DYE-terminater<sup>TM</sup> chemistry (PE Applied Biosystems, Foster City, CA, Cat. No: 403044) was used to sequence the PCR products with their respective PCR primers. The sequences were collected with an ABI377 instrument. For PCR products larger than 1kb, walking primers were used. The sequences of contigs generated by the OSS strategy in AutoAssembler<sup>TM</sup> (PE Applied Biosystems, Foster City, CA; Cat. No: 903227) and the gap-filling sequencing trace files were imported into Sequencher<sup>TM</sup> (Gene Codes Corp., Ann Arbor, MI) for overlapping and editing. The sequences generated by the total shotgun strategy were assembled using Phred and Phrap and edited using Consed (<http://chimera.biotech.washington.edu/uwgc/projects.htm>) and GFP (Genome Reconstruction Manager for Phrap), version 1.2 (<http://stork.cellb.bcm.tmc.edu/gfp/>).

#### PCR-Based gap filling Strategy:

Primers were designed based on the 5'- and 3'-end sequenced of each contig, avoiding repetitive and low quality sequence regions. All primers were designed to be 19-24-mers with 50-70% G/C content. Oligos were synthesized and gel-purified by standard methods.

Since the orientation and order of the contigs were unknown, permutations of the primers were used in the amplification reactions. Two PCR kits were used: first, XL PCR kit (Perkin Elmer, Norwalk, CT; Cat. No.: N8080205), with extension times of approximately 10 minutes; and second, the Taq polymerase PCR kit (Qiagen Inc., Valencia, CA; Cat. No.: 201223) was used under high stringency conditions if smeared or multiple products were observed with the XL PCR kit. The main PCR product from each successful reaction was extracted from a 0.9% low melting agarose gel and purified with the GeneClean DNA Purification kit prior to sequencing.

#### Analysis:

The identification and characterization of coding regions was carried out as follows: First, repetitive sequences were masked using RepeatMasker (A.F.A. Smit & P. Green, [http://ftp.genome.washington.edu/RM/RM\\_details.html](http://ftp.genome.washington.edu/RM/RM_details.html)) which screens DNA sequences in FastA format against a library of repetitive elements and returns a masked query sequence. Repeats not masked were identified by comparing the sequence to the GenBank database using WUBLAST2.0 [Altschul, S & Gish, W., Methods Enzymol. 266: 460-480 (1996); <http://blast.wustl.edu/blast/README.html>] and were masked manually.

Next, known genes were revealed by comparing the genomic regions against Genentech's protein database using the WUBLAST2.0 algorithm and then annotated by aligning the genomic and cDNA sequences for each gene, respectively, using a Needleman-Wunch (Needleman and Wunsch, J. Mol. Biol. 48: 443-453 (1970) algorithm to find regions of local identity between sequences. The strategy results in detection of all exons of the five known genes in the region, THPO, TRAP2, eIF4g, CLCN2 and hRPB17 (see below).

5

<u>Known genes</u>	<u>Map position</u>
eukaryotic translation initiation factor 4 gamma	3q27-qter
thrombopoietin	3q26-q27
chloride channel 2	3q26-qter
10 TNF receptor associated protein 2	not previously mapped
RNA polymerase II subunit hRPB17	not previously mapped

Finally, novel transcription units were predicted using a number of approaches. CpG islands (S. Cross & Bird, A., Curr. Opin. Genet. Dev. 5: 109-314 (1995) islands were used to define promoter regions and were identified as clusters of sites cleaved by enzymes recognizing GC-rich, 6 or 8-mer palindromic sequences (NotI, NarI, BssHII, XhoI. CpG islands are usually associated with promoter regions of genes. WUBLAST2.0 analysis of short genomic regions (10-20 kb) versus GenBank revealed matches to ESTs. The individual EST sequences (or where possible, their sequence chromatogram files) were retrieved and assembled with Sequencer to provide a theoretical cDNA sequence (DNA36443). GRAIL2 (ApoCom Inc., Knoxville, TN, command line version for the DEC alpha) was used to predict a novel exon. The five known genes in the region served as internal controls for the success of the GRAIL algorithm.

Isolation: A partial endothelin converting enzyme-2 (ECE-2) cDNA clone was isolated by first splicing in silico the ECE-2 exons predicted in the genomic sequence to generate a putative sequence (DNA36443). An oligonucleotide probe: GAAGCAGTGCAGCCAGCAGTAGAGAGGCACCTGCTAAGA) (SEQ ID NO:530) was designed and used to screen a human fetal small intestine library (LIB110) and internal PCR primers (36443f1) (ECE2.f:ACGCAGCTGGAGCTGGTCTTAGCA) (SEQ ID NO:531) and (36443r1) (ECE2.r) (GGTACTGGACCCCTAGGGCCACAA) (SEQ ID NO:532) were used to confirm clones hybridizing to the probe prior to sequencing. One positive clone was obtained, however this cDNA (DNA49830) represented a partially spliced transcript containing appropriately spliced exons 1 through 6, followed by intron 6 sequence. The oligo dT primer annealed to a polyA-stretch within an Alu element present in intron 6. An additional ECE-2 cDNA fragment (DNA49831) was obtained by PCR from a human fetal kidney library (LIB227) with primers designed from the presumed cDNA sequence [36443f3: CCTCCCAGCCGAGACCAAGTGG (SEQ ID NO:533) and 36443r2: GGTCTATAAGGGCCAAGACC (SEQ ID NO:534)]. This PCR product extended from exon 13 into the 3' untranslated region in exon 18.

A full length endothelin converting enzyme 2 (ECE-2) cDNA clone (DNA55800-1263) was isolated from an oligo-dT-primed human fetal brain library. RNA from human fetal brain tissue (20 weeks gestation, #283005)(SRC175) was isolated by guanidine thiocyanate and 5 µg used to generate double stranded cDNA which was cloned into the vector pRK5E. The 3' -primer (pGACTAGTTCTAGATCGCGAGCGGCCGCCCTTTTTTTTTTTTTT) (SEQ ID NO:535) and the 5 -linker (pCGGACGCGTGGGTCTGA) (SEQ ID NO:536) were designed to introduce XhoI and NotI restriction sites. The library was screened with PCR primers [36443pcrf1: CGGCCGTGATGGCTGGTGACG (SEQ ID NO:537) and 36443r3: GGCAGACTCCTTCCTATGGG (SEQ ID NO:538)] designed from the partial human ECE-2 cDNA sequences (DNA49830 and DNA49831). PCR products were cloned into the vector pCR2.1-TOPO (Invitrogen Corp., Carlsbad, CA, Cat. No. K4500-01) and sequenced with DYE-terminator chemistry as described above.

**EXAMPLE 98: Northern Blot and in situ RNA Hybridization Analysis for PRO403**

Expression of PRO403 mRNA in human tissues was examined by Northern blot analysis. Human polyA+ RNA blots derived from human fetal and adult tissues (Clontech, Palo Alto, CA; Cat. Nos. 7760-1, 7756-1 and 7755-1) were hybridized to a [32P-α]dATP-labelled cDNA fragments from probe based on the full length PRO403 cDNA. Blots were incubated with the probes in hybridization buffer (5X SSPE; 2X Denhardt's solution; 100 mg/mL denatured sheared salmon sperm DNA; 50% formamide; 2% SDS) for 18 hours at 42°C, washed to high stringency (0.1XSSC, 0.1% SDS, 50°C) and autoradiographed. The blots were developed after overnight exposure by phosphorimager analysis (Fuji).

PRO403 mRNA transcripts were detected. Analysis of the expression pattern showed the strongest signal of the expected 3.3 kb transcript in adult brain (highest in the cerebellum, putamen, medulla, and temporal lobe, and lower in the cerebral cortex, occipital lobe and frontal lobe), spinal cord, lung and pancreas and higher levels of a 4.5 kb transcript in fetal brain and kidney.

**EXAMPLE 99: Use of PRO Polypeptide-Encoding Nucleic Acid as Hybridization Probes**

The following method describes use of a nucleotide sequence encoding a PRO polypeptide as a hybridization probe.

DNA comprising the coding sequence of of a PRO polypeptide of interest as disclosed herein may be employed as a probe or used as a basis from which to prepare probes to screen for homologous DNAs (such as those encoding naturally-occurring variants of the PRO polypeptide) in human tissue cDNA libraries or human tissue genomic libraries.

Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO polypeptide-encoding nucleic acid-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO polypeptide can then be identified using standard techniques known in the art.

**EXAMPLE 100: Expression of PRO Polypeptides in *E. coli***

This example illustrates preparation of an unglycosylated form of a desired PRO polypeptide by recombinant expression in *E. coli*.

The DNA sequence encoding the desired PRO polypeptide is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the specific PRO polypeptide coding region, lambda transcriptional terminator, and an argU gene.

The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO polypeptide can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO181, PRO195, PRO200, PRO237, PRO273, PRO540, PRO322, PRO1017, PRO938, PRO162, PRO1114, PRO827 and PRO1008 were expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding the PRO polypeptide was initially amplified using selected PCR primers. The primers contained restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences were then ligated into an expression vector, which was used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants were first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 was reached. Cultures were then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, 0.71 g sodium citrate·2H<sub>2</sub>O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as

110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM  $\text{MgSO}_4$ ) and grown for approximately 20-30 hours at 30°C with shaking. Samples were removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets were frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) was resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution was stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution was centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant was diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. Depending the clarified extract was loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column was washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein was eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein were pooled and stored at 4°C. Protein concentration was estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins were refolded by diluting sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes were chosen so that the final protein concentration was between 50 to 100 micrograms/ml. The refolding solution was stirred gently at 4°C for 12-36 hours. The refolding reaction was quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution was filtered through a 0.22 micron filter and acetonitrile was added to 2-10% final concentration. The refolded protein was chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A<sub>280</sub> absorbance were analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein were pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO proteins were pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins were formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

#### EXAMPLE 101: Expression of PRO Polypeptides in Mammalian Cells

This example illustrates preparation of a glycosylated form of a desired PRO polypeptide by recombinant expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector.

Optionally, the PRO polypeptide-encoding DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO polypeptide DNA using ligation methods such as described in Sambrook et al., supra. The resulting vector is called pRK5-PRO polypeptide.

In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10  $\mu$ g pRK5-PRO polypeptide DNA is mixed with about 1  $\mu$ g DNA encoding the VA RNA gene [Thimmappaya et al., Cell, 31:543 (1982)] and dissolved in 500  $\mu$ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M  $\text{CaCl}_2$ . To this mixture is added, dropwise, 500  $\mu$ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM  $\text{NaPO}_4$ , and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200  $\mu$ Ci/ml  $^{35}\text{S}$ -cysteine and 200  $\mu$ Ci/ml  $^{35}\text{S}$ -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO polypeptide may be introduced into 293 cells transiently using the dextran sulfate method described by Somparyrac et al., Proc. Natl. Acad. Sci., 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700  $\mu$ g pRK5-PRO polypeptide DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5  $\mu$ g/ml bovine insulin and 0.1  $\mu$ g/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO polypeptide can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO polypeptides can be expressed in CHO cells. The pRK5-PRO polypeptide can be transfected into CHO cells using known reagents such as  $\text{CaPO}_4$  or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as  $^{35}\text{S}$ -methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO polypeptide can then be concentrated and purified by any selected method.

Epitope-tagged PRO polypeptide may also be expressed in host CHO cells. The PRO polypeptide may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO polypeptide

insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO polypeptide can then be concentrated and purified by any selected method, such as by Ni<sup>2+</sup>-chelate affinity chromatography.

- 5 Stable expression in CHO cells was performed using the following procedure. The proteins were expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins were fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

- Following PCR amplification, the respective DNAs were subcloned in a CHO expression vector using  
10 standard techniques as described in Ausubel et al., *Current Protocols of Molecular Biology*, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., *Nucl. Acids Res.* 24: 9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR  
15 expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA were introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect\* (Quiagen), Dospert\* or Fugene\* (Boehringer Mannheim). The cells were grown and described in Lucas et al., supra. Approximately 3 x 10<sup>7</sup> cells are frozen in an ampule for further growth and production as described below.

- 20 The ampules containing the plasmid DNA were thawed by placement into water bath and mixed by vortexing. The contents were pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant was aspirated and the cells were resuspended in 40 mL of selective media (0.2 µm filtered PS20 with 5% 0.2 µm diafiltered fetal bovine serum). The cells were then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells were transferred into a 250 mL  
25 spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, a 250 mL, 500 mL and 2000 mL spinners were seeded with 3 x 10<sup>5</sup> cells/mL. The cell media was exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in US Patent No. 5,122,469, issued June 16, 1992 was actually used. 3L production spinner is seeded at 1.2 x 10<sup>6</sup> cells/mL. On day 0, the cell number pH were determined. On day  
30 1, the spinner was sampled and sparging with filtered air was commenced. On day 2, the spinner was sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion). Throughout the production, pH was adjusted as necessary to keep at around 7.2. After 10 days, or until viability dropped below 70%, the cell culture was harvested by centrifugation and filtering through a 0.22 µm filter. The filtrate was either stored at  
35 4°C or immediately loaded onto columns for purification.



For the poly-His tagged constructs, the proteins were purified using a Ni-NTA column (Qiagen). Before purification, imidazole was added to the conditioned media to a concentration of 5 mM. The conditioned media was pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column was washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein was subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc containing) constructs were purified from the conditioned media as follows. The conditioned medium was pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column was washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein was immediately neutralized by collecting 1 ml fractions into tubes containing 275 µL of 1 M Tris buffer, pH 9. The highly purified protein was subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity was assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

The following PRO polypeptides were successfully transiently expressed in CHO cells: PRO200, PRO320, PRO237, PRO273, PRO337, PRO846, PRO363, PRO322, PRO1083, PRO938, PRO1012, PRO1114, PRO1008 and PRO1075.

The following PRO polypeptides were successfully transiently expressed in COS cells: PRO181, PRO195, PRO200, PRO320, PRO237, PRO273, PRO285, PRO337, PRO526, PRO540, PRO846, PRO362, PRO363, PRO700, PRO707, PRO617, PRO322, PRO719, PRO1083, PRO868, PRO866, PRO768, PRO938, PRO1012, PRO162, PRO1114, PRO827, PRO1008 and PRO1075.

The following PRO polypeptides were successfully stably expressed in CHO cells: PRO181, PRO195, PRO200, PRO320, PRO285, PRO337, PRO846, PRO362, PRO363, PRO707, PRO617, PRO322, PRO1083, PRO868, PRO866, PRO1017, PRO792, PRO788, PRO938, PRO1012, PRO162, PRO1114, PRO827, PRO1008, PRO1075 and PRO1031.

#### EXAMPLE 102: Expression of PRO Polypeptides in Yeast

The following method describes recombinant expression of a desired PRO polypeptide in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO polypeptides from the ADH2/GAPDH promoter. DNA encoding a desired PRO polypeptide, a selected signal peptide and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of the PRO polypeptide. For secretion, DNA encoding the PRO polypeptide can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, the yeast alpha-factor secretory signal/leader sequence, and linker sequences (if needed) for expression of the PRO polypeptide.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with

Coomassie Blue stain.

Recombinant PRO polypeptide can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing the PRO polypeptide may further be purified using selected column chromatography resins.

5

**EXAMPLE 103: Expression of PRO Polypeptides in Baculovirus-Infected Insect Cells**

The following method describes recombinant expression of PRO polypeptides in Baculovirus-infected insect cells.

The desired PRO polypeptide is fused upstream of an epitope tag contained with a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the PRO polypeptide or the desired portion of the PRO polypeptide (such as the sequence encoding the extracellular domain of a transmembrane protein) is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4-5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression is performed as described by O'Reilley et al., Baculovirus expression vectors: A laboratory Manual, Oxford: Oxford University Press (1994).

Expressed poly his tagged PRO polypeptides can then be purified, for example, by Ni<sup>2+</sup>-NTA affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., *Nature*, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl<sub>2</sub>; 0.1 mM EDTA; 10% Glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% Glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni<sup>2+</sup>-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A<sub>280</sub> with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% Glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A<sub>280</sub> baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or western blot with Ni<sup>2+</sup>-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His<sub>10</sub>-tagged PRO polypeptide are pooled and dialyzed against loading buffer.

Alternatively, purification of the IgG tagged (or Fc tagged) PRO polypeptide can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

PRO195, PRO526, PRO540, PRO846, PRO362, PRO363, PRO700, PRO707, PRO322, PRO719, PRO1083, PRO868, PRO866, PRO768, PRO788, PRO938, PRO827 and PRO1031 were successfully expressed in baculovirus infected Sf9 insect cells. While the expression was actually performed in a 0.5-2 L scale, it can be readily scaled up for larger (e.g. 8 L) preparations. The proteins were expressed as an IgG construct (immunoadhesin), in which the protein extracellular region was fused to an IgG1 constant region sequence containing the hinge, CH2 and CH3 domains and/or in poly-His tagged forms.

For expression in baculovirus infected Sf9 cells, following PCR amplification, the respective coding sequences were subcloned into a baculovirus expression vector (pb.PH.IgG for IgG fusions and pb.PH.His.c for poly-His tagged proteins), and the vector and Baculogold® baculovirus DNA (Pharmingen) were co-transfected into 105 *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711), using Lipofectin (Gibco BRL). pb.PH.IgG and pb.PH.His are modifications of the commercially available baculovirus expression vector pVL1393 (Pharmingen), with modified polylinker regions to include the His or Fc tag sequences. The cells were grown in Hink's TNM-FH medium supplemented with 10% FBS (Hyclone). Cells were incubated for 5 days at 28°C. The supernatant was harvested and subsequently used for the first viral amplification by infecting Sf9 cells in Hink's TNM-FH medium supplemented with 10% FBS at an approximate multiplicity of infection (MOI) of 10. Cells were incubated for 3 days at 28°C. The supernatant was harvested and the expression of the constructs in the baculovirus expression vector was determined by batch binding of 1 ml of supernatant to 25 mL of Ni-NTA beads (QIAGEN) for histidine tagged proteins or Protein-A Sepharose CL-4B beads (Pharmacia) for IgG tagged proteins followed by SDS-PAGE analysis comparing to a known concentration of protein standard by Coomassie blue staining.

The first viral amplification supernatant was used to infect a spinner culture (500 mL) of Sf9 cells grown in ESF-921 medium (Expression Systems LLC) at an approximate MOI of 0.1. Cells were incubated for 3 days at 28°C. The supernatant was harvested and filtered. Batch binding and SDS-PAGE analysis was repeated, as necessary, until expression of the spinner culture was confirmed.

The conditioned medium from the transfected cells (0.5 to 3 L) was harvested by centrifugation to remove the cells and filtered through 0.22 micron filters. For the poly-His tagged constructs, the protein construct were purified using a Ni-NTA column (Qiagen). Before purification, imidazole was added to the conditioned media to a concentration of 5 mM. The conditioned media were pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column was washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein was subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc containing) constructs of proteins were purified from the conditioned media as follows. The conditioned media were pumped onto a 5 ml Protein A column (Pharmacia) which had been

equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column was washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein was immediately neutralized by collecting 1 ml fractions into tubes containing 275 mL of 1 M Tris buffer, pH 9. The highly purified protein was subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity of the proteins was verified by SDS polyacrylamide gel (PAGE) electrophoresis and N-terminal amino acid sequencing by Edman degradation.

PRO181, PRO195, PRO200, PRO320, PRO237, PRO273, PRO285, PRO337, PRO526, PRO540, PRO846, PRO362, PRO363, PRO617, PRO322, PRO1083, PRO868, 768, PRO792, PRO788, PRO162, PRO1114, PRO827, PRO1075 and PRO1031 were successfully expressed in baculovirus infected Hi5 insect cells. While the expression was actually performed in a 0.5-2 L scale, it can be readily scaled up for larger (e.g. 8 L) preparations.

For expression in baculovirus-infected Hi5 insect cells, the PRO polypeptide-encoding DNA may be amplified with suitable systems, such as Pfu (Stratagene), or fused upstream (5'-of) of an epitope tag contained with a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the PRO polypeptide or the desired portion of the PRO polypeptide (such as the sequence encoding the extracellular domain of a transmembrane protein) is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector. For example, derivatives of pVL1393 can include the Fc region of human IgG (pb.PH.IgG) or an 8 histidine (pb.PH.His) tag downstream (3'-of) the NAME sequence. Preferably, the vector construct is sequenced for confirmation.

Hi5 cells are grown to a confluency of 50% under the conditions of 27°C, 5% CO<sub>2</sub>, NO pen/strep. For each 150 mm plate, 30 ug of pIE based vector containing PRO polypeptide is mixed with 1 ml Ex-Cell medium (Media: Ex-Cell 401 + 1/100 L-Glu JRH Biosciences #14401-78P (note: this media is light sensitive)), and in a separate tube, 100 ul of CellFectin (CellFECTIN (GibcoBRL #10362-010) (vortexed to mix)) is mixed with 1 ml of Ex-Cell medium. The two solutions are combined and allowed to incubate at room temperature for 15 minutes. 8 ml of Ex-Cell media is added to the 2ml of DNA/CellFECTIN mix and this is layered on Hi5 cells that have been washed once with Ex-Cell media. The plate is then incubated in darkness for 1 hour at room temperature. The DNA/CellFECTIN mix is then aspirated, and the cells are washed once with Ex-Cell to remove excess CellFECTIN. 30 ml of fresh Ex-Cell media is added and the cells are incubated for 3 days at 28°C. The supernatant is harvested and the expression of the PRO polypeptide in the baculovirus expression vector can be determined by batch binding of 1 ml of supernatant to 25 mL of Ni-NTA beads (QIAGEN) for histidine tagged proteins or Protein-A Sepharose CL-4B beads (Pharmacia) for IgG tagged proteins followed by SDS-PAGE analysis comparing to a known concentration of protein standard by Coomassie blue staining.

The conditioned media from the transfected cells (0.5 to 3 L) is harvested by centrifugation to remove the cells and filtered through 0.22 micron filters. For the poly-His tagged constructs, the protein comprising

the PRO polypeptide is purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc containing) constructs of proteins are purified from the conditioned media as follows. The conditioned media is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 mL of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity of PRO polypeptide can be assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation and other analytical procedures as desired or necessary.

#### EXAMPLE 104: Preparation of Antibodies that Bind to PRO Polypeptides

This example illustrates preparation of monoclonal antibodies which can specifically bind to a PRO polypeptide.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO polypeptide, fusion proteins containing the PRO polypeptide, and cells expressing recombinant PRO polypeptide on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO polypeptide immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO polypeptide antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO polypeptide. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against the PRO polypeptide. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against the PRO polypeptide is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO polypeptide monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

10 EXAMPLE 105: Chimeric PRO Polypeptides

PRO polypeptides may be expressed as chimeric proteins with one or more additional polypeptide domains added to facilitate protein purification. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAG<sup>SM</sup> extension/affinity purification system (Immunex Corp., Seattle Wash.). The inclusion of a cleavable linker sequence such as Factor XA or enterokinase (Invitrogen, San Diego Calif.) between the purification domain and the PRO polypeptide sequence may be useful to facilitate expression of DNA encoding the PRO polypeptide.

20 EXAMPLE 106: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE<sup>TM</sup> (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may

be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., a low pH buffer such as approximately pH 2-3, or a high concentration  
5 of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

#### EXAMPLE 107: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed  
10 in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO  
15 polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and  
20 the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

25 Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art.  
30 Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO  
35 polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

**EXAMPLE 108: Rational Drug Design**

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

**EXAMPLE 109: Ability of PRO Polypeptides to Inhibit Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth**

The ability of various PRO polypeptides to inhibit VEGF stimulated proliferation of endothelial cells was tested. Specifically, bovine adrenal cortical capillary endothelial (ACE) cells (from primary culture, maximum 12-14 passages) were plated on 96-well microtiter plates (Amersham Life Science) at a density of 500 cells/well per 100  $\mu$ L in low glucose DMEM, 10% calf serum, 2 mM glutamine, 1x pen/strept and fungizone, supplemented with 3 ng/mL VEGF. Controls were plated the same way but some did not include VEGF. A test sample of the PRO polypeptide of interest was added in a 100  $\mu$ L volume for a 200  $\mu$ L final volume. Cells were incubated for 6-7 days at 37°C. The media was aspirated and the cells washed 1x with PBS. An acid



phosphatase reaction mixture (100  $\mu$ L, 0.1M sodium acetate, pH 5.5, 0.1% Triton-100, 10 mM p-nitrophenyl phosphate) was added. After incubation for 2 hours at 37°C, the reaction was stopped by addition of 10  $\mu$ L 1N NaOH. OD was measured on microtiter plate reader at 405 nm. Controls were no cells, cells alone, cells + FGF (5 ng/mL), cells + VEGF (3 ng/mL), cells + VEGF (3 ng/mL) + TGF- $\beta$  (1 ng/mL), and cells + VEGF (3 ng/mL) + LIF (5 ng/mL). (TGF- $\beta$  at a 1 ng/mL concentration is known to block 70-90% of VEGF stimulated cell proliferation.)

The results were assessed by calculating the percentage inhibition of VEGF (3 ng/mL) stimulated cells proliferation, determined by measuring acid phosphatase activity at OD405 nm, (1) relative to cells without stimulation, and (2) relative to the reference TGF- $\beta$  inhibition of VEGF stimulated activity. The results are indicative of the utility of the PRO polypeptides in cancer therapy and specifically in inhibiting tumor angiogenesis.

The PRO polypeptides demonstrated as being capable of inhibiting VEGF stimulated proliferation of endothelial cell growth at various concentrations include PRO200 and PRO320.

#### EXAMPLE 110: Retinal Neuron Survival

This example demonstrates that various PRO polypeptides have efficacy in enhancing the survival of retinal neuron cells.

Sprague Dawley rat pups at postnatal day 7 (mixed population: glia and retinal neuronal types) are killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N2 and with or without the specific PRO polypeptide. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are stained with calcein AM then fixed using 4% paraformaldehyde and stained with DAPI for determination of total cell count. The total cells (fluorescent) are quantified at 20X objective magnification using CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

The effect of various concentration of PRO polypeptides is calculated by dividing the total number of calcein AM positive cells at 2-3 days in culture by the total number of DAPI-labeled cells at 2-3 days in culture. Anything above 30% survival is considered positive. The following PRO polypeptides were positive in this assay: PRO200, PRO540, PRO846 and PRO617.

#### EXAMPLE 111: Rod Photoreceptor Survival

This example demonstrates that various PRO polypeptides have efficacy in enhancing the survival of rod photoreceptor cells.

Sprague Dawley rat pups at 7 day postnatal (mixed population: glia and retinal neuronal cell types) are

killed by decapitation following CO<sub>2</sub> anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca<sup>2+</sup>, Mg<sup>2+</sup>-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N2 and with or without the specific test PRO polypeptide. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO<sub>2</sub>. After 2-3 days in culture, cells are fixed using 4% paraformaldehyde, and then stained using CellTracker Green CMFDA. Rho 4D2 (ascites or IgG 1:100), a monoclonal antibody directed towards the visual pigment rhodopsin is used to detect rod photoreceptor cells by indirect immunofluorescence. The results are reported as % survival: total number of calcein/CellTracker - rhodopsin positive cells at 2-3 days in culture, divided by the total number of rhodopsin positive cells at time 2-3 days in culture. The total cells (fluorescent) are quantified at 20x objective magnification using a CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

With regard to the effect of various concentration of PRO polypeptides, anything above 10% survival is considered positive. The following PRO polypeptides tested positive in this assay: PRO200, PRO540, PRO846 and PRO617.

EXAMPLE 112: Ability of PRO Polypeptides to Stimulate the Release of Proteoglycans from Cartilage

The ability of various PRO polypeptides to stimulate the release of proteoglycans from cartilage tissue was tested as follows.

The metacarpophalangeal joint of 4-6 month old pigs was aseptically dissected, and articular cartilage was removed by free hand slicing being careful to avoid the underlying bone. The cartilage was minced and cultured in bulk for 24 hours in a humidified atmosphere of 95% air, 5% CO<sub>2</sub> in serum free (SF) media (DME/F12 1:1) with 0.1% BSA and 100U/ml penicillin and 100µg/ml streptomycin. After washing three times, approximately 100 mg of articular cartilage was aliquoted into microtubes and incubated for an additional 24 hours in the above SF media. PRO polypeptides were then added at 1% either alone or in combination with 18 ng/ml interleukin-1α, a known stimulator of proteoglycan release from cartilage tissue. The supernatant was then harvested and assayed for the amount of proteoglycans using the 1,9-dimethyl-methylene blue (DMB) colorimetric assay (Farndale and Buttle, *Biochem. Biophys. Acta* 883:173-177 (1985)). A positive result in this assay indicates that the test polypeptide will find use, for example, in the treatment of sports-related joint problems, articular cartilage defects, osteoarthritis or rheumatoid arthritis.

When PRO200 polypeptides were tested in the above assay, the polypeptides demonstrated a marked ability to stimulate release of proteoglycans from cartilage tissue both basally and after stimulation with interleukin-1α and at 24 and 72 hours after treatment, thereby indicating that PRO200 polypeptides are useful for stimulating proteoglycan release from cartilage tissue.

**EXAMPLE 113: In Vitro Antiproliferative Assay**

The antiproliferative activity of various PRO polypeptides was determined in the investigational, disease-oriented *in vitro* anti-cancer drug discovery assay of the National Cancer Institute (NCI), using a sulforhodamine B (SRB) dye binding assay essentially as described by Skehan et al., *J. Natl. Cancer Inst.* 82:1107-1112 (1990). The 60 tumor cell lines employed in this study ("the NCI panel"), as well as conditions  
5 for their maintenance and culture *in vitro* have been described by Monks et al., *J. Natl. Cancer Inst.* 83:757-766 (1991). The purpose of this screen is to initially evaluate the cytotoxic and/or cytostatic activity of the test compounds against different types of tumors (Monks et al., *supra*; Boyd, *Cancer: Princ. Pract. Oncol. Update* 3(10):1-12 [1989]).

Cells from approximately 60 human tumor cell lines were harvested with trypsin/EDTA (Gibco),  
10 washed once, resuspended in IMEM and their viability was determined. The cell suspensions were added by pipet (100  $\mu$ L volume) into separate 96-well microtiter plates. The cell density for the 6-day incubation was less than for the 2-day incubation to prevent overgrowth. Inoculates were allowed a preincubation period of 24 hours at 37°C for stabilization. Dilutions at twice the intended test concentration were added at time zero in 100  $\mu$ L aliquots to the microtiter plate wells (1:2 dilution). Test compounds were evaluated at five half-log dilutions  
15 (1000 to 100,000-fold). Incubations took place for two days and six days in a 5% CO<sub>2</sub> atmosphere and 100% humidity.

After incubation, the medium was removed and the cells were fixed in 0.1 ml of 10% trichloroacetic acid at 40°C. The plates were rinsed five times with deionized water, dried, stained for 30 minutes with 0.1 ml of 0.4% sulforhodamine B dye (Sigma) dissolved in 1% acetic acid, rinsed four times with 1% acetic acid to  
20 remove unbound dye, dried, and the stain was extracted for five minutes with 0.1 ml of 10 mM Tris base [tris(hydroxymethyl)aminomethane], pH 10.5. The absorbance (OD) of sulforhodamine B at 492 nm was measured using a computer-interfaced, 96-well microtiter plate reader.

A test sample is considered positive if it shows at least 50% growth inhibitory effect at one or more concentrations. The following PRO polypeptides gave positive results in at least one tumor cell line: PRO181,  
25 PRO237, PRO526, PRO362 and PRO866.

**EXAMPLE 114: Gene Amplification**

This example shows that genes encoding various PRO polypeptides are amplified in the genome of certain human cancers. Amplification is associated with overexpression of the gene product, indicating that the  
30 PRO polypeptide is a useful target for therapeutic intervention in certain cancers such as colon, lung and other cancers. Therapeutic agent may take the form of antagonists of PRO polypeptide-encoding genes, for example, murine-human chimeric, humanized or human antibodies against the PRO polypeptide.

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, e.g., fluorometrically. As a negative control, DNA was isolated from the cells of ten  
35 normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (NorHu).

The 5' nuclease assay (for example, TaqMan™) and real-time quantitative PCR (for example, ABI Prizm 7700 Sequence Detection System™ (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding the PRO polypeptide is over-represented in any of the lung and colon cancers that were screened. The result was reported in Delta CT units. One unit corresponds 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold and so on. Quantitation was obtained using primers and a Taqman™ fluorescent derived from the PRO polypeptide-encoding gene. Regions of the PRO polypeptide which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are preferred for the primer derivation, e.g., 3'-untranslated region.

The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor amplification in real time. Two oligonucleotide primers are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe, is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the probe is cleaved by the Taq DNA polymerase enzyme in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI Prism 7700™ Sequence Detection. The system consists of a thermocycler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5' Nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The Ct values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample.

Genes encoding the following PRO polypeptides were found to be amplified in the above assay:  
PRO213-1, PRO237, PRO324, PRO351, PRO362, PRO853, PRO615, PRO531, PRO618, PRO772, PRO703, PRO474, PRO1017 and PRO792.

#### EXAMPLE 115: Induction of c-fos in Endothelial Cells

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50:50 without glycine, 1% glutamine, 10mM Hepes, 10% FBS, 10 ng/ml bFGF), were plated on 96-well microtiter plates at a cell density of  $1 \times 10^4$  cells/well. The day after plating, the cells were starved by removing the growth media

and treating the cells with 100  $\mu$ l/well test samples and controls (positive control: growth media; negative control: Protein 32). The cells were incubated for 30 minutes at 37°C, in 5% CO<sub>2</sub>. The samples were removed, and the first part of the bDNA kit protocol (Chiron Diagnostics, cat. #6005-037) was followed.

Briefly, the amounts of the TM Lysis Buffer and Probes needed for the tests were calculated based on information provided by the manufacturer. The appropriate amounts of thawed Probes were added to the TM Lysis Buffer. The Capture Hybridization Buffer was warmed to room temperature. The bDNA strips were set up in the metal strip holders, and 100  $\mu$ l of Capture Hybridization Buffer were added to each b-DNA well needed, followed by incubation for at least 30 minutes. The test plates with the cells were removed from the incubator, and the media was gently removed using the vacuum manifold. 100 $\mu$ l of Lysis Hybridization Buffer with Probes were quickly pipetted into each well of the microtiter plates. The plates were then incubated at 55°C for 15 minutes. Upon removal from the incubator, the plates were placed on the vortex mixer with the microtiter adapter head and vortex on the #2 setting for one minute. 80  $\mu$ l of the lysate were removed and added to the bDNA wells containing the Capture Hybridization Buffer, and pipetted up and down to mix. The plates were incubated at 53°C for at least 16 hours.

On the next day, the second part of the bDNA kit protocol was followed. Specifically, the Plates were removed from the incubator and placed on the bench to cool for 10 minutes. The volumes of additions needed were calculated based upon information provided by the manufacturer. An Amplifier Working Solution was prepared by making a 1:100 dilution of the Amplifier Concentrate (20 fm/ $\mu$ l) in AL Hybridization Buffer. The hybridization mixture was removed from the plates and washed twice with Wash A. 50  $\mu$ l of Amplifier Working Solution were added to each well and the wells were incubated at 53°C for 30 minutes. The plates were then removed from the incubator and allowed to cool for 10 minutes. The Label Probe Working Solution was prepared by making a 1:100 dilution of Label Concentrate (40 pmoles/ $\mu$ l) in AL Hybridization Buffer. After the 10 minutes cool down period, the amplifier hybridization mixture was removed and the plates washed twice with Wash A. 50 $\mu$ l of Label Probe Working Solution were added to each well and the wells were incubated at 53°C for 15 minutes. After cooling for 10 minutes, the Substrate was warmed to room temperature. Upon addition of 3  $\mu$ l of Substrate Enhancer to each ml of Substrate needed for the assay, the plates were allowed to cool for 10 minutes, the label hybridization mixture was removed, and the plates were washed twice with Wash A and three-times with Wash D. 50 $\mu$ l of the Substrate Solution with Enhancer were added to each well. The plates were incubated for 30 minutes at 37°C and RLU read in an appropriate luminometer.

The replicates were averaged and the coefficient of variation was determined. The measure of activity of the fold increase over the Protein 32 (buffer control) value indicated by chemoluminescence units (RLU). Samples which showed an at least two-fold value over the Protein 32 value were considered positive. PRO938 was positive in the above assay.

#### EXAMPLE 116: Proliferation of Rat Utricular Supporting Cells

In an effort to identify PRO polypeptides that act as potent mitogens for inner ear supporting cells which are hair cell progenitors (related to auditory hair cell regeneration), various PRO polypeptides were tested in the

following assay.

The rat utricular epithelial cell line (UEC-4 cells) are aliquoted into 96 well plates with a density of 3000 cells/well in 200  $\mu$ l of serum-containing medium at 33°C. After overnight, the cultures are switched to serum-free medium at 37°C and the PRO polypeptide samples are added at various dilutions. After 24h incubation, <sup>3</sup>H-thymidine (1  $\mu$ Ci/well) is added to the cultures for an additional 24h. The cells are then harvested using a Tomtec cell harvester. Because the epithelial cells are grown on a polylysine substrate, trypsin (1 mg/ml) is added to the culture wells for 30 min at 37°C to lift the cells before cell harvest. Cpm/well are counted with a matrix 9600 gas counter (Packard Instrument Company, Downers Grove, IL). Data is collected from 3 culture wells from each of the experimental groups and expressed as mean  $\pm$  SEM. A two-tailed, unpaired t-test is used for statistical analysis, as compared to the control group (treatment with TGF- $\alpha$ ).

Average cpm counts which are at least 30% higher than the control values are considered positive for the assay. The following PRO polypeptides were positive in this assay: PRO337, PRO363 and PRO1012.

#### EXAMPLE 117: *In situ* Hybridization

*In situ* hybridization is a powerful and versatile technique for the detection and localization of nucleic acid sequences within cell or tissue preparations. It may be useful, for example, to identify sites of gene expression, analyze the tissue distribution of transcription, identify and localize viral infection, follow changes in specific mRNA synthesis and aid in chromosome mapping.

*In situ* hybridization was performed following an optimized version of the protocol by Lu and Gillett, Cell Vision 1:169-176 (1994), using PCR-generated <sup>32</sup>P-labeled riboprobes. Briefly, formalin-fixed, paraffin-embedded human tissues were sectioned, deparaffinized, deproteinized in proteinase K (20 g/ml) for 15 minutes at 37°C, and further processed for *in situ* hybridization as described by Lu and Gillett, *supra*. A [<sup>32</sup>P] UTP-labeled antisense riboprobe was generated from a PCR product and hybridized at 55°C overnight. The slides were dipped in Kodak NTB2 nuclear track emulsion and exposed for 4 weeks.

#### <sup>32</sup>P-Riboprobe synthesis

6.0  $\mu$ l (125 mCi) of <sup>32</sup>P-UTP (Amersham BF 1002, SA < 2000 Ci/mmol) were speed vac dried. To each tube containing dried <sup>32</sup>P-UTP, the following ingredients were added:

2.0  $\mu$ l 5x transcription buffer

1.0  $\mu$ l DTT (100 mM)

2.0  $\mu$ l NTP mix (2.5 mM : 10  $\mu$ ; each of 10 mM GTP, CTP & ATP + 10  $\mu$ l H<sub>2</sub>O)

1.0  $\mu$ l UTP (50  $\mu$ M)

1.0  $\mu$ l Rnasin

1.0  $\mu$ l DNA template (1  $\mu$ g)

1.0  $\mu$ l H<sub>2</sub>O

1.0  $\mu$ l RNA polymerase (for PCR products T3 = AS, T7 = S, usually)

The tubes were incubated at 37°C for one hour. 1.0  $\mu$ l RQ1 DNase were added, followed by incubation at 37°C for 15 minutes. 90  $\mu$ l TE (10 mM Tris pH 7.6/1mM EDTA pH 8.0) were added, and the mixture was

pipetted onto DE81 paper. The remaining solution was loaded in a Microcon-50 ultrafiltration unit, and spun using program 10 (6 minutes). The filtration unit was inverted over a second tube and spun using program 2 (3 minutes). After the final recovery spin, 100  $\mu$ l TE were added. 1  $\mu$ l of the final product was pipetted on DE81 paper and counted in 6 ml of Biofluor II.

The probe was run on a TBE/urea gel. 1-3  $\mu$ l of the probe or 5  $\mu$ l of RNA Mrk III were added to 3  $\mu$ l of loading buffer. After heating on a 95°C heat block for three minutes, the gel was immediately placed on ice. The wells of gel were flushed, the sample loaded, and run at 180-250 volts for 45 minutes. The gel was wrapped in saran wrap and exposed to XAR film with an intensifying screen in -70°C freezer one hour to overnight.

### <sup>32</sup>P-Hybridization

#### 10 A. Pretreatment of frozen sections

The slides were removed from the freezer, placed on aluminium trays and thawed at room temperature for 5 minutes. The trays were placed in 55°C incubator for five minutes to reduce condensation. The slides were fixed for 10 minutes in 4% paraformaldehyde on ice in the fume hood, and washed in 0.5 x SSC for 5 minutes, at room temperature (25 ml 20 x SSC + 975 ml SQ H<sub>2</sub>O). After deproteinization in 0.5  $\mu$ g/ml proteinase K for 10 minutes at 37°C (12.5  $\mu$ l of 10 mg/ml stock in 250 ml prewarmed RNase-free RNase buffer), the sections were washed in 0.5 x SSC for 10 minutes at room temperature. The sections were dehydrated in 70%, 95%, 100% ethanol, 2 minutes each.

#### B. Pretreatment of paraffin-embedded sections

The slides were deparaffinized, placed in SQ H<sub>2</sub>O, and rinsed twice in 2 x SSC at room temperature, for 5 minutes each time. The sections were deproteinated in 20  $\mu$ g/ml proteinase K (500  $\mu$ l of 10 mg/ml in 250 ml RNase-free RNase buffer; 37°C, 15 minutes) - human embryo, or 8 x proteinase K (100  $\mu$ l in 250 ml RNase buffer, 37°C, 30 minutes) - formalin tissues. Subsequent rinsing in 0.5 x SSC and dehydration were performed as described above.

#### C. Prehybridization

The slides were laid out in a plastic box lined with Box buffer (4 x SSC, 50% formamide) - saturated filter paper. The tissue was covered with 50  $\mu$ l of hybridization buffer (3.75g Dextran Sulfate + 6 ml SQ H<sub>2</sub>O), vortexed and heated in the microwave for 2 minutes with the cap loosened. After cooling on ice, 18.75 ml formamide, 3.75 ml 20 x SSC and 9 ml SQ H<sub>2</sub>O were added, the tissue was vortexed well, and incubated at 42°C for 1-4 hours.

#### 30 D. Hybridization

1.0 x 10<sup>6</sup> cpm probe and 1.0  $\mu$ l tRNA (50 mg/ml stock) per slide were heated at 95°C for 3 minutes. The slides were cooled on ice, and 48  $\mu$ l hybridization buffer were added per slide. After vortexing, 50  $\mu$ l <sup>32</sup>P mix were added to 50  $\mu$ l prehybridization on slide. The slides were incubated overnight at 55°C.

#### E. Washes

35 Washing was done 2 x 10 minutes with 2xSSC, EDTA at room temperature (400 ml 20 x SSC + 16 ml 0.25M EDTA, V<sub>T</sub>=4L), followed by RNaseA treatment at 37°C for 30 minutes (500  $\mu$ l of 10 mg/ml in 250

ml Rnase buffer = 20 µg/ml). The slides were washed 2 x 10 minutes with 2 x SSC, EDTA at room temperature. The stringency wash conditions were as follows: 2 hours at 55°C, 0.1 x SSC, EDTA (20 ml 20 x SSC + 16 ml EDTA, V<sub>T</sub>=4L).

F. Oligonucleotides

*In situ* analysis was performed on a variety of DNA sequences disclosed herein. The oligonucleotides employed for these analyses were derived from the nucleotide sequences disclosed herein and generally range from about 40 to 55 nucleotides in length.

G. Results

*In situ* analysis was performed on a variety of DNA sequences disclosed herein. The results from these analyses are as follows.

10 (1) DNA29101-1122 (PRO200)

Fetal: Lower limb expression in developing lower limb bones at the edge of the cartilagenous anlage (i.e. around the outside edge); in developing tendons, in vascular smooth muscle and in cells embracing developing skeletal muscle myocytes and myotubes. Expression also observed at the epiphyseal growth plate. Lymph node expression in marginal sinus of developing lymph nodes. Thymus expression in the subcapsular region of the thymic cortex, possibly representing either the subcapsular epithelial cells or the proliferating, double negative, thymocytes that are found in this region. Spleen is negative. Trachea expression in smooth muscle. Brain (cerebral cortex) focal expression in cortical neurones. Spinal cord negative. Small intestine expression in smooth muscle. Thyroid - generalized expression over thyroid epithelium. Adrenal is negative. Liver expression in ductal plate cells. Stomach expression in mural smooth muscle. Fetal skin expression in basal layer of squamous epithelium. Placenta expression in interstitial cells in trophoblastic villi. Cord expression in wall of arteries and vein.

Comments: Expression pattern suggests that PRO200 may be involved in cell differentiation/proliferation.

High expression was observed at the following additional sites: Chimp ovary - granulosa cells of maturing follicles, lower intensity signal observed over thecal cells. Chimp parathyroid - high expression over chief cells. Human fetal testis - moderate expression over stromal cells surrounding developing tubules. Human fetal lung - high expression over chondrocytes in developing bronchial tree, and low level expression over branching bronchial epithelium. Specific expression was not observed over the renal cell, gastric and colonic carcinomas. Fetal tissues examined (E12-E16 weeks) include: placenta, umbilical cord, liver, kidney, adrenals, thyroid, lungs, heart, great vessels, oesophagus, stomach, small intestine, spleen, thymus, pancreas, brain, eye, spinal cord, body wall, pelvis and lower limb. Adult tissues examined: liver, kidney, adrenal, myocardium, aorta, spleen, lymph node, pancreas, lung, skin, cerebral cortex (rm), hippocampus(rm), cerebellum(rm), penis, eye, bladder, stomach, gastric carcinoma, colon, colonic carcinoma and chondrosarcoma. Acetaminophen induced liver injury and hepatic cirrhosis.

35



(2) DNA30867-1335 (PRO218)

Low level expression over numerous epithelia including fetal small intestine, fetal thyroid, chimp gastric epithelium. Expression also seen over malignant cells in a renal cell carcinoma. Expression in fetal brain, over cortex. The distribution does not suggest an obvious function. Human fetal tissues examined (E12-E16 weeks) include: placenta, umbilical cord, liver, kidney, adrenals, thyroid, lungs, heart, great vessels, oesophagus, stomach, small intestine, spleen, thymus, pancreas, brain, eye, spinal cord, body wall, pelvis and lower limb. Adult human tissues examined: kidney (normal and end-stage), bladder, adrenal, spleen, lymph node, pancreas, lung, skin, eye (inc. retina), colon, bladder, liver (normal, cirrhotic, acute failure), heart, clear cell carcinoma of kidney, gastric adenocarcinoma, colorectal carcinoma. Non-human primate tissues examined: Chimp tissues: salivary gland, stomach, thyroid, parathyroid, tongue, thymus, ovary, lymph node, peripheral nerve. Rhesus Monkey tissues: cerebral cortex, hippocampus, cerebellum, penis.

(3) DNA40021-1154 (PRO285)

Low levels of expression observed in the placenta and over hematopoietic cells in the mouse fetal liver. No expression was detected in either human fetal, adult or chimp lymph node and no expression was detected in human fetal or human adult spleen. Fetal tissues examined (E12-E16 weeks) include: placenta, umbilical cord, liver, kidney, adrenals, thyroid, lungs, heart, great vessels, oesophagus, stomach, small intestine, spleen, thymus, pancreas, brain, eye, spinal cord, body wall, pelvis and lower limb. Adult tissues examined: liver, kidney, adrenal, myocardium, aorta, spleen, lymph node, pancreas, lung, skin, cerebral cortex (rm), hippocampus(rm), cerebellum(rm), brain infarct (human), cerebritis (human), penis, eye, bladder, stomach, gastric carcinoma, colon, colonic carcinoma, thyroid (chimp), parathyroid (chimp) ovary (chimp) and chondrosarcoma. Acetaminophen induced liver injury and hepatic cirrhosis.

(4) DNA39523-1192 (PRO273)

Expression over epithelium of mouse embryo skin as well as over basal epithelium and dermis of human fetal skin. Basal epithelial pegs of the squamous mucosa of the chimp tongue are also positive. Expression over a subset of cells in developing glomeruli of fetal kidney, adult renal tubules, and over "thyroidized" epithelium in end-stage renal disease, low expression in a renal cell carcinoma, probably over the epithelial cells. Low level expression over stromal cells in fetal lung. Expression over stromal cells in the apical portion of gastric glands. High expression in the lamina propria of the fetal small intestinal villi, normal colonic mucosa and over stromal cells in a colonic carcinoma. Strong expression over benign connective tissue cells in the hyalinized stroma of a sarcoma. Expression over stromal cells in the placental villi and the splenic red pulp. In the brain, expression over cortical neurones. Connective tissue surrounding developing bones and over nerve sheath cells in the fetus. Fetal tissues examined (E12-E16 weeks) include: placenta, umbilical cord, liver, kidney, adrenals, thyroid, lungs, heart, great vessels, oesophagus, stomach, small intestine, spleen, thymus, pancreas, brain, eye, spinal cord, body wall, pelvis and lower limb. Adult tissues examined: liver, kidney, adrenal, myocardium, aorta, spleen, lymph node, pancreas, lung, skin, cerebral cortex (rm), hippocampus(rm), eye, stomach, gastric

carcinoma, colon, colonic carcinoma, thyroid (chimp), parathyroid (chimp) ovary (chimp) and chondrosarcoma. Acetaminophen induced liver injury and hepatic cirrhosis.

Expression was present in many cells in the outer layers (I and II) of the monkey cerebral cortex. A small subset of cells in the deeper cortical layers also expressed mRNA for this chemokine homolog. Scattered cells within the molecular layers of the hippocampus and bordering the inner edge of the dentate gyrus contained chemokine homolog mRNA. No expression was detected within the cerebellar cortex. Chemokine homolog expression is not observed in infarcted brain, where cell death has occurred in the regions where the chemokine homolog normally is expressed. This probe could possibly serve as a marker of a subset of neurons of outer layers of the cerebral cortex and could possibly reveal neuronal migration disorders. Abnormal neuronal migration is a possible cause of some seizure disorders and schizophrenia. In order to gain a better appreciation of the distribution of this mRNA we will test whether the probe will cross-hybridize with mouse brain tissue.

Also shows intriguing and specific patterns of hybridization within postnatal day (P)10 and adult mouse brains. In one sagittal section of P10 mouse brain, strong signal was observed scattered within the molecular layer of the hippocampus and inner edges of the dentate gyrus. Cells in the presubiculum were moderately labeled; the signal extended in a strong band through outer layers of the retrosplenial cortex to the occipital cortex, where the signal diminished to background levels. A small set of positive neurons were detected in deeper regions of P10 motor cortex; neurons in outer layers of P10 cortex did not exhibit signal above background levels. Moderate hybridization signal was also detected in the inferior colliculus. Chemokine homolog signal in the adult mouse brain was evaluated in three coronal sections at different levels. Strong signal was detected in the septum and in scattered neurons in the pontine nuclei and motor root of the trigeminal nerve; moderate signal was seen in the molecular layers of the hippocampus and outer layers of the retrosplenial cortex.

(5) DNA39979-1213 (PRO296)

Widespread expression in fetal in adult tissues. Expressed in a variety of fetal and adult epithelia, skeletal and cardiac muscle, developing (including retina) and adult CNS, thymic epithelium, placental villi, hepatocytes in cirrhotic and acetaminophen induced toxicity. Highly expressed in hypertrophic chondrocytes in developing skeletal system. The overall expression pattern, while not completely overlapping (not expressed in glomeruli, more widely expressed in CNS), is not dissimilar to VEGF. A possible role in angiogenesis should therefore be considered. Human fetal tissues examined (E12-E16 weeks) include: placenta, umbilical cord, liver, kidney, adrenals, thyroid, lungs, great vessels, stomach, small intestine, spleen, thymus, pancreas, brain, eye, spinal cord, body wall, pelvis, testis and lower limb. Adult human tissues examined: kidney (normal and end-stage), adrenal, spleen, lymph node, pancreas, lung, eye (inc. retina), bladder, liver (normal, cirrhotic, acute failure). Non-human primate tissues examined: Chimp tissues: adrenal. Rhesus Monkey tissues: cerebral cortex, hippocampus, cerebellum.

(6) DNA52594-1270 (PRO868)

Expression over neuronal cells in fetal dorsal root ganglia, spinal cord, developing enteric neurons, cortical neurons. Low level expression also seen in placental trophoblast. In adult tissues the only site where notable expression was observed was the normal adult prostate; as such it may represent a possible prostate cell surface receptor target antigen. Studies to further characterize the expression in adult tissues seem warranted.

- 5 Low level expression also observed in a liposarcoma. Fetal tissues examined (E12-E16 weeks) include: placenta, umbilical cord, liver, kidney, adrenals, thyroid, lungs, heart, great vessels, oesophagus, stomach, small intestine, spleen, thymus, pancreas, brain, eye, spinal cord, body wall, pelvis and lower limb. Adult human tissues examined: liver, kidney, adrenal, myocardium, aorta, spleen, lung, skin, chondrosarcoma, eye, stomach, gastric carcinoma, colon, colonic carcinoma, renal cell carcinoma, prostate, bladder mucosa and gall bladder.
- 10 Acetaminophen induced liver injury and hepatic cirrhosis. Rhesus tissues examined: cerebral cortex (rm), hippocampus(rm), cerebellum. Chimp tissues examined: thyroid, parathyroid, ovary, nerve, tongue, thymus, adrenal, gastric mucosa and salivary gland. WIG-1(WISP-1), WIG-2 (WISP-2) and WIG-5 (WISP-3) expression in human breast carcinoma and normal breast tissue, Wig-2 in lung carcinoma, and Wig-5 in colon carcinoma.

15 (7) DNA64907-1163 (PRO1330)

- In human fetal tissues there was strong specific expression over arterial, venous, capillary and sinusoidal endothelium in all tissues examined, except for fetal brain. In normal adult tissues expression was low to absent, but when present appeared expression was confined to the vasculature. Highest expression in adult tissues was observed regionally in vessels running within the white matter of rhesus brain - the significance
- 20 of this pattern is unclear. Elevated expression observed in vasculature of many inflamed and diseased tissues, including tumor vasculature. In some of these tissues it was unclear if expression was solely confined to vascular endothelium. In the 15 lung tumors examined no expression was seen over the malignant epithelium, however, vascular expression was observed in many of the tumors and adjacent lung tissue. Moderate, apparently non-specific background, was seen with this probe over hyalinised collagen and sites of tissue necrosis. In the
- 25 absence of a sense control, however, it is not possible to be absolutely certain that all of this signal is non-specific. Some signal, also thought to be non-specific, was seen over the chimp gastric mucosa, transitional cell epithelium of human adult bladder and fetal retina.

(8) DNA49624-1279 (PRO545)

- 30 Expression of the ADAM family molecule, ADAM 12 (DNA49624-1279) observed in normal human lung, lung tumor, normal colon and colon carcinoma.

(9) DNA59294-1381 (PRO1031)

- The expression of this IL17 homologue was evaluated in a panel consisting of normal adult and fetal
- 35 tissues and tissues with inflammation, predominantly chronic lymphocytic inflammation. This panel is designed to specifically evaluate the expression pattern in immune mediated inflammatory disease of novel proteins that

modulate T lymphocyte function (stimulatory or inhibitory). This protein when expressed as an Ig-fusion protein was immunostimulatory in a dose dependent fashion in the human mixed lymphocyte reaction (MLR); it caused a 285% and 147% increase above the baseline stimulation index when utilized at two different concentrations (1.0% and 0.1% of a 560 nM stock). Summary: expression was restricted to muscle, certain types of smooth muscle in the adult and in skeletal and smooth muscle in the human fetus. Expression in adult human was in smooth muscle of tubular organs evaluated including colon and gall bladder. There no expression in the smooth muscle of vessels or bronchi. No adult human skeletal muscle was evaluated. In fetal tissues there was moderate to high diffuse expression in skeletal muscle the axial skeleton and limbs. There was weak expression in the smooth muscle of the intestinal wall but no expression in cardiac muscle. Adult human tissues with expression: Colon. there was low level diffuse expression in the smooth muscle (tunica muscularis) in 5 specimens with chronic inflammatory bowel disease. Gall bladder: there was weak to low level expression in the smooth muscle of the gall bladder. Fetal human tissues with expression: there was moderate diffuse expression in skeletal muscle and weak to low expression in smooth muscle; there was no expression in fetal heart or any other fetal organ including liver, spleen, CNS, kidney, gut, lung. Human tissues with no expression: lung with chronic granulomatous inflammation and chronic bronchitis (5 patients), peripheral nerve, prostate, heart, placenta, liver (disease multiblock), brain (cerebrum and cerebellum), tonsil (reactive hyperplasia), peripheral lymph node, thymus.

(10) DNA45416-1251 (PRO362)

The expression of this novel protein was evaluated in a variety of human and non-human primate tissues and was found to be highly restricted. Expression was present only in alveolar macrophages in the lung and in Kupffer cells of the hepatic sinusoids. Expression in these cells was significantly increased when these distinct cell populations were activated. Though these two subpopulations of tissue macrophages are located in different organs, they have similar biological functions. Both types of these phagocytes act as biological filters to remove material from the blood stream or airways including pathogens, senescent cells and proteins and both are capable of secreting a wide variety of important proinflammatory cytokines. In inflamed lung (7 patient samples) expression was prominent in reactive alveolar macrophage cell populations defined as large, pale often vacuolated cells present singly or in aggregates within alveoli and was weak to negative in normal, non-reactive macrophages (single scattered cells of normal size). Expression in alveolar macrophages was increased during inflammation when these cells were both increased in numbers and size (activated). Despite the presence of histocytes in areas of interstitial inflammation and peribronchial lymphoid hyperplasia in these tissues, expression was restricted to alveolar macrophages. Many of the inflamed lungs also had some degree of suppurative inflammation; expression was not present in neutrophilic granulocytes. In liver, there was strong expression in reactive/activated Kupffer cells in livers with acute centrilobular necrosis (acetaminophen toxicity) or fairly marked periportal inflammation. However there was weak or no expression in Kupffer cells in normal liver or in liver with only mild inflammation or mild to moderate lobular hyperplasia/hypertrophy. Thus, as in the lung, there was increased expression in activated/reactive cells. There was no expression of this molecule in histiocytes/macrophages present in inflamed bowel, hyperplastic/reactive tonsil or normal lymph node. The lack

of expression in these tissues which all contained histiocytic inflammation or resident macrophage populations strongly supports restricted expression to the unique macrophage subset populations defined as alveolar macrophage and hepatic Kupffer cells. Spleen or bone marrow was not available for evaluation. Human tissues evaluated which had no detectable expression included: Inflammatory bowel disease (7 patient samples with moderate to severe disease), tonsil with reactive hyperplasia, peripheral lymphnode, psoriatic skin (2 patient samples with mild to moderate disease), heart, peripheral nerve. Chimp tissues evaluated which had no detectable expression included: tongue, stomach, thymus.

(11) DNA52196-1348 (PRO733)

Generalized low level signal in many tissues and in many cell types. While endothelial cell expression was observed it was not a prominent feature in either fetal, normal or diseased tissues. Human tissues: moderate expression over fetal liver (mainly hepatocytes), lung, skin, adrenal and heart. Fetal spleen, small intestine, brain and eye are negative. Adult normal kidney, bladder epithelium, lung, adrenal, pancreas, skin - all negative. Expression in adult human liver (normal and diseased), renal tubules in end-stage renal disease, adipose tissue, sarcoma, colon, renal cell carcinoma, hepatocellular carcinoma, squamous cell carcinoma. Non human primate tissues: chimp salivary gland, vessels, stomach, tongue, peripheral nerve, thymus, lymph node, thyroid and parathyroid. Rhesus spinal cord negative, cortical and hippocampal neurones positive.

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 12301

20 Parklawn Drive, Rockville, MD, USA (ATCC):

Material	ATCC Dep. No.	Deposit Date
DNA39967-1184	ATCC 209786	April 21, 1998
DNA40625-1189	ATCC 209788	April 21, 1998
DNA23318-1211	ATCC 209787	April 21, 1998
25 DNA39979-1213	ATCC 209789	April 21, 1998
DNA40594-1233	ATCC 209617	February 5, 1998
DNA45416-1251	ATCC 209620	February 5, 1998
DNA45419-1252	ATCC 209616	February 5, 1998
DNA52594-1270	ATCC 209679	March 17, 1998
30 DNA45234-1277	ATCC 209654	March 5, 1998
DNA49624-1279	ATCC 209655	March 5, 1998
DNA48309-1280	ATCC 209656	March 5, 1998
DNA46776-1284	ATCC 209721	March 31, 1998
DNA50980-1286	ATCC 209717	March 31, 1998
35 DNA50913-1287	ATCC 209716	March 31, 1998
DNA50914-1289	ATCC 209722	March 31, 1998
DNA48296-1292	ATCC 209668	March 11, 1998
DNA32284-1307	ATCC 209670	March 11, 1998
DNA36343-1310	ATCC 209718	March 31, 1998
40 DNA40571-1315	ATCC 209784	April 21, 1998
DNA41386-1316	ATCC 209703	March 26, 1998
DNA44194-1317	ATCC 209808	April 28, 1998
DNA45415-1318	ATCC 209810	April 28, 1998

	DNA44189-1322	ATCC 209699	March 26, 1998
	DNA48304-1323	ATCC 209811	April 28, 1998
	DNA49152-1324	ATCC 209813	April 28, 1998
	DNA49646-1327	ATCC 209705	March 26, 1998
	DNA49631-1328	ATCC 209806	April 28, 1998
5	DNA49645-1347	ATCC 209809	April 28, 1998
	DNA45493-1349	ATCC 209805	April 28, 1998
	DNA48227-1350	ATCC 209812	April 28, 1998
	DNA41404-1352	ATCC 209844	May 6, 1998
	DNA44196-1353	ATCC 209847	May 6, 1998
10	DNA52187-1354	ATCC 209845	May 6, 1998
	DNA48328-1355	ATCC 209843	May 6, 1998
	DNA56352-1358	ATCC 209846	May 6, 1998
	DNA53971-1359	ATCC 209750	April 7, 1998
	DNA50919-1361	ATCC 209848	May 6, 1998
15	DNA44179-1362	ATCC 209851	May 6, 1998
	DNA54002-1367	ATCC 209754	April 7, 1998
	DNA53906-1368	ATCC 209747	April 7, 1998
	DNA52185-1370	ATCC 209861	May 14, 1998
	DNA53977-1371	ATCC 209862	May 14, 1998
20	DNA57253-1382	ATCC 209867	May 14, 1998
	DNA58847-1383	ATCC 209879	May 20, 1998
	DNA58747-1384	ATCC 209868	May 14, 1998
	DNA57689-1385	ATCC 209869	May 14, 1998
	DNA23330-1390	ATCC 209775	April 14, 1998
25	DNA26847-1395	ATCC 209772	April 14, 1998
	DNA53974-1401	ATCC 209774	April 14, 1998
	DNA57039-1402	ATCC 209777	April 14, 1998
	DNA57033-1403	ATCC 209905	May 27, 1998
	DNA34353-1428	ATCC 209855	May 12, 1998
30	DNA45417-1432	ATCC 209910	May 27, 1998
	DNA39523-1192	ATCC 209424	October 31, 1997
	DNA44205-1285	ATCC 209720	March 31, 1998
	DNA50911-1288	ATCC 209714	March 31, 1998
	DNA48329-1290	ATCC 209785	April 21, 1998
35	DNA48306-1291	ATCC 209911	May 27, 1998
	DNA48336-1309	ATCC 209669	March 11, 1998
	DNA44184-1319	ATCC 209704	March 26, 1998
	DNA48314-1320	ATCC 209702	March 26, 1998
	DNA48333-1321	ATCC 209701	March 26, 1998
40	DNA50920-1325	ATCC 209700	March 26, 1998
	DNA50988-1326	ATCC 209814	April 28, 1998
	DNA48331-1329	ATCC 209715	March 31, 1998
	DNA30867-1335	ATCC 209807	April 28, 1998
	DNA55737-1345	ATCC 209753	April 7, 1998
45	DNA49829-1346	ATCC 209749	April 7, 1998
	DNA52196-1348	ATCC 209748	April 7, 1998
	DNA56965-1356	ATCC 209842	May 6, 1998
	DNA56405-1357	ATCC 209849	May 6, 1998
	DNA57530-1375	ATCC 209880	May 20, 1998
50	DNA56439-1376	ATCC 209864	May 14, 1998
	DNA56409-1377	ATCC 209882	May 20, 1998
	DNA56112-1379	ATCC 209883	May 20, 1998
	DNA56045-1380	ATCC 209865	May 14, 1998
	DNA59294-1381	ATCC 209866	May 14, 1998

	DNA56433-1406	ATCC 209857	May 12, 1998
	DNA53912-1457	ATCC 209870	May 14, 1998
	DNA50921-1458	ATCC 209859	May 12, 1998
	DNA29101-1122	ATCC 209653	March 5, 1998
	DNA40021-1154	ATCC 209389	October 17, 1997
5	DNA42663-1154	ATCC 209386	October 17, 1997
	DNA30943-1-1163-1	ATCC 209791	April 21, 1998
	DNA64907-1163-1	ATCC 203242	September 9, 1998
	DNA64908-1163-1	ATCC 203243	September 9, 1998
	DNA39975-1210	ATCC 209783	April 21, 1998
10	DNA43316-1237	ATCC 209487	November 21, 1997
	DNA55800-1263	ATCC 209680	March 17, 1998

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC § 122 and the Commissioner's rules pursuant thereto (including 37 CFR § 1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:7), Figure 9 (SEQ ID NO:19), Figure 11 (SEQ ID NO:28), Figure 15 (SEQ ID NO:36), Figure 20 (SEQ ID NO:45), Figure 22 (SEQ ID NO:52), Figure 24 (SEQ ID NO:59), Figure 26 (SEQ ID NO:64), Figure 28 (SEQ ID NO:69), Figure 30 (SEQ ID NO:74), Figure 33 (SEQ ID NO:85), Figure 35 (SEQ ID NO:90), Figure 37 (SEQ ID NO:97), Figure 39 (SEQ ID NO:102), Figure 41 (SEQ ID NO:109), Figure 43 (SEQ ID NO:114), Figure 45 (SEQ ID NO:119), Figure 47 (SEQ ID NO:124), Figure 49 (SEQ ID NO:132), Figure 51 (SEQ ID NO:137), Figure 53 (SEQ ID NO:145), Figure 55 (SEQ ID NO:150), Figure 59 (SEQ ID NO:157), Figure 61 (SEQ ID NO:162), Figure 63 (SEQ ID NO:169), Figure 66 (SEQ ID NO:178), Figure 68 (SEQ ID NO:183), Figure 70 (SEQ ID NO:190), Figure 73 (SEQ ID NO:196), Figure 75 (SEQ ID NO:206), Figure 77 (SEQ ID NO:211), Figure 79 (SEQ ID NO:216), Figure 81 (SEQ ID NO:221), Figure 83 (SEQ ID NO:226), Figure 85 (SEQ ID NO:231), Figure 87 (SEQ ID NO:236), Figure 89 (SEQ ID NO:245), Figure 91 (SEQ ID NO:254), Figure 93 (SEQ ID NO:259), Figure 95 (SEQ ID NO:264), Figure 98 (SEQ ID NO:270), Figure 109 (SEQ ID NO:284), Figure 118 (SEQ ID NO:296), Figure 120 (SEQ ID NO:301), Figure 122 (SEQ ID NO:303), Figure 125 (SEQ ID NO:309), Figure 129 (SEQ ID NO:322), Figure 132 (SEQ ID NO:330), Figure 136 (SEQ ID NO:337), Figure 139 (SEQ ID NO:346), Figure 142 (SEQ ID NO:352), Figure 145 (SEQ ID NO:358), Figure 147 (SEQ ID NO:363), Figure 149 (SEQ ID NO:370), Figure 151 (SEQ ID NO:375), Figure 153 (SEQ ID NO:380), Figure 155 (SEQ ID NO:385), Figure 157 (SEQ ID NO:390), Figure 159 (SEQ ID NO:395), Figure 161 (SEQ ID NO:400), Figure 163 (SEQ ID NO:405), Figure 165 (SEQ ID NO:410), Figure 167 (SEQ ID NO:415), Figure 169 (SEQ ID NO:420), Figure 171 (SEQ ID NO:425), Figure 173 (SEQ ID NO:430), Figure 177 (SEQ ID NO:437), Figure 179 (SEQ ID NO:442), Figure 181 (SEQ ID NO:447), Figure 183 (SEQ ID NO:452), Figure 185 (SEQ ID NO:454), Figure 187 (SEQ ID NO:456), Figure 190 (SEQ ID NO:459), Figure 192 (SEQ ID NO:464), Figure 194 (SEQ ID NO:466), Figure 196 (SEQ ID NO:468), Figure 198 (SEQ ID NO:470), Figure 200 (SEQ ID NO:472), Figure 202 (SEQ ID NO:477), Figure 204 (SEQ ID NO:483), Figure 207 (SEQ ID NO:488), Figure 209 (SEQ ID NO:496), Figure 211 (SEQ ID NO:498), Figure 213 (SEQ ID NO:506), Figure 215 (SEQ ID NO:508), Figure 217 (SEQ ID NO:510), Figure 219 (SEQ ID NO:515), Figure 222 (SEQ ID NO:523) and Figure 225 (SEQ ID NO:526).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:6), Figure 8 (SEQ ID NO:18), Figure 10 (SEQ ID NO:27), Figure 14 (SEQ ID NO:35), Figure 19 (SEQ ID NO:44), Figure 21 (SEQ ID NO:51), Figure 23 (SEQ ID NO:58), Figure 25 (SEQ ID NO:63), Figure 27 (SEQ ID NO:68), Figure 29 (SEQ ID NO:73), Figure 32 (SEQ ID NO:84), Figure 34 (SEQ ID NO:89), Figure 36 (SEQ ID NO:96), Figure 38 (SEQ ID NO:101), Figure 40 (SEQ ID NO:108), Figure 42 (SEQ ID NO:113), Figure 44 (SEQ ID NO:118), Figure 46 (SEQ ID NO:123), Figure 48 (SEQ ID NO:131), Figure 50 (SEQ ID



NO:136), Figure 52 (SEQ ID NO:144), Figure 54 (SEQ ID NO:149), Figure 58 (SEQ ID NO:156), Figure 60 (SEQ ID NO:161), Figure 62 (SEQ ID NO:168), Figure 65 (SEQ ID NO:177), Figure 67 (SEQ ID NO:182), Figure 69 (SEQ ID NO:189), Figure 72 (SEQ ID NO:195), Figure 74 (SEQ ID NO:205), Figure 76 (SEQ ID NO:210), Figure 78 (SEQ ID NO:215), Figure 80 (SEQ ID NO:220), Figure 82 (SEQ ID NO:225), Figure 84 (SEQ ID NO:230), Figure 86 (SEQ ID NO:235), Figure 88 (SEQ ID NO:244), Figure 90 (SEQ ID NO:253),  
 5 Figure 92 (SEQ ID NO:258), Figure 94 (SEQ ID NO:263), Figure 97 (SEQ ID NO:269), Figure 108 (SEQ ID NO:283), Figure 117 (SEQ ID NO:295), Figure 119 (SEQ ID NO:300), Figure 121 (SEQ ID NO:302), Figure 124 (SEQ ID NO:308), Figure 128 (SEQ ID NO:321), Figure 131 (SEQ ID NO:329), Figure 135 (SEQ ID NO:336), Figure 138 (SEQ ID NO:345), Figure 141 (SEQ ID NO:351), Figure 144 (SEQ ID NO:357), Figure 146 (SEQ ID NO:362), Figure 148 (SEQ ID NO:369), Figure 150 (SEQ ID NO:374), Figure 152 (SEQ ID  
 10 NO:379), Figure 154 (SEQ ID NO:384), Figure 156 (SEQ ID NO:389), Figure 158 (SEQ ID NO:394), Figure 160 (SEQ ID NO:399), Figure 162 (SEQ ID NO:404), Figure 164 (SEQ ID NO:409), Figure 166 (SEQ ID NO:414), Figure 168 (SEQ ID NO:419), Figure 170 (SEQ ID NO:424), Figure 172 (SEQ ID NO:429), Figure 176 (SEQ ID NO:436), Figure 178 (SEQ ID NO:441), Figure 180 (SEQ ID NO:446), Figure 182 (SEQ ID NO:451), Figure 184 (SEQ ID NO:453), Figure 186 (SEQ ID NO:455), Figure 189 (SEQ ID NO:458), Figure  
 15 191 (SEQ ID NO:463), Figure 193 (SEQ ID NO:465), Figure 195 (SEQ ID NO:467), Figure 197 (SEQ ID NO:469), Figure 199 (SEQ ID NO:471), Figure 201 (SEQ ID NO:476), Figure 203 (SEQ ID NO:482), Figure 206 (SEQ ID NO:487), Figure 208 (SEQ ID NO:495), Figure 210 (SEQ ID NO:497), Figure 212 (SEQ ID NO:505), Figure 214 (SEQ ID NO:507), Figure 216 (SEQ ID NO:509), Figure 218 (SEQ ID NO:514), Figure 221 (SEQ ID NO:522) and Figure 224 (SEQ ID NO:525).

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3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:6), Figure 8 (SEQ ID NO:18), Figure 10 (SEQ ID NO:27), Figure 14 (SEQ ID NO:35), Figure 19 (SEQ ID NO:44), Figure 21 (SEQ ID NO:51), Figure 23 (SEQ ID NO:58), Figure 25 (SEQ ID NO:63), Figure 27 (SEQ ID NO:68), Figure 29 (SEQ ID NO:73), Figure 32 (SEQ ID NO:84), Figure  
 25 34 (SEQ ID NO:89), Figure 36 (SEQ ID NO:96), Figure 38 (SEQ ID NO:101), Figure 40 (SEQ ID NO:108), Figure 42 (SEQ ID NO:113), Figure 44 (SEQ ID NO:118), Figure 46 (SEQ ID NO:123), Figure 48 (SEQ ID NO:131), Figure 50 (SEQ ID NO:136), Figure 52 (SEQ ID NO:144), Figure 54 (SEQ ID NO:149), Figure 58 (SEQ ID NO:156), Figure 60 (SEQ ID NO:161), Figure 62 (SEQ ID NO:168), Figure 65 (SEQ ID NO:177),  
 30 Figure 67 (SEQ ID NO:182), Figure 69 (SEQ ID NO:189), Figure 72 (SEQ ID NO:195), Figure 74 (SEQ ID NO:205), Figure 76 (SEQ ID NO:210), Figure 78 (SEQ ID NO:215), Figure 80 (SEQ ID NO:220), Figure 82 (SEQ ID NO:225), Figure 84 (SEQ ID NO:230), Figure 86 (SEQ ID NO:235), Figure 88 (SEQ ID NO:244), Figure 90 (SEQ ID NO:253), Figure 92 (SEQ ID NO:258), Figure 94 (SEQ ID NO:263), Figure 97 (SEQ ID NO:269), Figure 108 (SEQ ID NO:283), Figure 117 (SEQ ID NO:295), Figure 119 (SEQ ID NO:300), Figure  
 35 121 (SEQ ID NO:302), Figure 124 (SEQ ID NO:308), Figure 128 (SEQ ID NO:321), Figure 131 (SEQ ID NO:329), Figure 135 (SEQ ID NO:336), Figure 138 (SEQ ID NO:345), Figure 141 (SEQ ID NO:351), Figure

144 (SEQ ID NO:357), Figure 146 (SEQ ID NO:362), Figure 148 (SEQ ID NO:369), Figure 150 (SEQ ID NO:374), Figure 152 (SEQ ID NO:379), Figure 154 (SEQ ID NO:384), Figure 156 (SEQ ID NO:389), Figure 158 (SEQ ID NO:394), Figure 160 (SEQ ID NO:399), Figure 162 (SEQ ID NO:404), Figure 164 (SEQ ID NO:409), Figure 166 (SEQ ID NO:414), Figure 168 (SEQ ID NO:419), Figure 170 (SEQ ID NO:424), Figure 172 (SEQ ID NO:429), Figure 176 (SEQ ID NO:436), Figure 178 (SEQ ID NO:441), Figure 180 (SEQ ID NO:446), Figure 182 (SEQ ID NO:451), Figure 184 (SEQ ID NO:453), Figure 186 (SEQ ID NO:455), Figure 189 (SEQ ID NO:458), Figure 191 (SEQ ID NO:463), Figure 193 (SEQ ID NO:465), Figure 195 (SEQ ID NO:467), Figure 197 (SEQ ID NO:469), Figure 199 (SEQ ID NO:471), Figure 201 (SEQ ID NO:476), Figure 203 (SEQ ID NO:482), Figure 206 (SEQ ID NO:487), Figure 208 (SEQ ID NO:495), Figure 210 (SEQ ID NO:497), Figure 212 (SEQ ID NO:505), Figure 214 (SEQ ID NO:507), Figure 216 (SEQ ID NO:509), Figure 218 (SEQ ID NO:514), Figure 221 (SEQ ID NO:522) or Figure 224 (SEQ ID NO:525).

4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under accession number ATCC 209791, ATCC 209786, ATCC 209788, ATCC 209787, ATCC 209789, ATCC 209617, ATCC 209620, ATCC 209616, ATCC 209679, ATCC 209654, ATCC 209655, ATCC 209656, ATCC 209721, ATCC 209717, ATCC 209716, ATCC 209722, ATCC 209668, ATCC 209670, ATCC 209718, ATCC 209784, ATCC 209703, ATCC 209808, ATCC 209810, ATCC 209699, ATCC 209811, ATCC 209813, ATCC 209705, ATCC 209806, ATCC 209809, ATCC 209805, ATCC 209812, ATCC 209844, ATCC 209847, ATCC 209845, ATCC 209843, ATCC 209846, ATCC 209750, ATCC 209848, ATCC 209851, ATCC 209754, ATCC 209747, ATCC 209861, ATCC 209862, ATCC 209867, ATCC 209879, ATCC 209868, ATCC 209869, ATCC 209775, ATCC 209772, ATCC 209774, ATCC 209777, ATCC 209905, ATCC 209855, ATCC 209910, ATCC 209424, ATCC 209720, ATCC 209714, ATCC 209785, ATCC 209911, ATCC 209669, ATCC 209704, ATCC 209702, ATCC 209701, ATCC 209700, ATCC 209814, ATCC 209715, ATCC 209807, ATCC 209755, ATCC 209749, ATCC 209748, ATCC 209842, ATCC 209849, ATCC 209880, ATCC 209864, ATCC 209882, ATCC 209883, ATCC 209865, ATCC 209866, ATCC 209857, ATCC 209870, ATCC 209859, ATCC 209653, ATCC 209389, ATCC 209386, ATCC 203242, ATCC 203243, ATCC 209783, ATCC 209487 or ATCC 209680.

5. A vector comprising the nucleic acid of Claim 1.

6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.

7. A host cell comprising the vector of Claim 5.

8. The host cell of Claim 7 wherein said cell is a CHO cell.

9. The host cell of Claim 7 wherein said cell is an *E. coli*.

10. The host cell of Claim 7 wherein said cell is a yeast cell.

11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

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12. Isolated native sequence PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:7), Figure 9 (SEQ ID NO:19), Figure 11 (SEQ ID NO:28), Figure 15 (SEQ ID NO:36), Figure 20 (SEQ ID NO:45), Figure 22 (SEQ ID NO:52), Figure 24 (SEQ ID NO:59), Figure 26 (SEQ ID NO:64), Figure 28 (SEQ ID NO:69), Figure 30 (SEQ ID NO:74), Figure 33 (SEQ ID NO:85), Figure 35 (SEQ ID NO:90), Figure 37 (SEQ ID NO:97), Figure 39 (SEQ ID NO:102), Figure 41 (SEQ ID NO:109), Figure 43 (SEQ ID NO:114), Figure 45 (SEQ ID NO:119), Figure 47 (SEQ ID NO:124), Figure 49 (SEQ ID NO:132), Figure 51 (SEQ ID NO:137), Figure 53 (SEQ ID NO:145), Figure 55 (SEQ ID NO:150), Figure 59 (SEQ ID NO:157), Figure 61 (SEQ ID NO:162), Figure 63 (SEQ ID NO:169), Figure 66 (SEQ ID NO:178), Figure 68 (SEQ ID NO:183), Figure 70 (SEQ ID NO:190), Figure 73 (SEQ ID NO:196), Figure 75 (SEQ ID NO:206), Figure 77 (SEQ ID NO:211), Figure 79 (SEQ ID NO:216), Figure 81 (SEQ ID NO:221), Figure 83 (SEQ ID NO:226), Figure 85 (SEQ ID NO:231), Figure 87 (SEQ ID NO:236), Figure 89 (SEQ ID NO:245), Figure 91 (SEQ ID NO:254), Figure 93 (SEQ ID NO:259), Figure 95 (SEQ ID NO:264), Figure 98 (SEQ ID NO:270), Figure 109 (SEQ ID NO:284), Figure 118 (SEQ ID NO:296), Figure 120 (SEQ ID NO:301), Figure 122 (SEQ ID NO:303), Figure 125 (SEQ ID NO:309), Figure 129 (SEQ ID NO:322), Figure 132 (SEQ ID NO:330), Figure 136 (SEQ ID NO:337), Figure 139 (SEQ ID NO:346), Figure 142 (SEQ ID NO:352), Figure 145 (SEQ ID NO:358), Figure 147 (SEQ ID NO:363), Figure 149 (SEQ ID NO:370), Figure 151 (SEQ ID NO:375), Figure 153 (SEQ ID NO:380), Figure 155 (SEQ ID NO:385), Figure 157 (SEQ ID NO:390), Figure 159 (SEQ ID NO:395), Figure 161 (SEQ ID NO:400), Figure 163 (SEQ ID NO:405), Figure 165 (SEQ ID NO:410), Figure 167 (SEQ ID NO:415), Figure 169 (SEQ ID NO:420), Figure 171 (SEQ ID NO:425), Figure 173 (SEQ ID NO:430), Figure 177 (SEQ ID NO:437), Figure 179 (SEQ ID NO:442), Figure 181 (SEQ ID NO:447), Figure 183 (SEQ ID NO:452), Figure 185 (SEQ ID NO:454), Figure 187 (SEQ ID NO:456), Figure 190 (SEQ ID NO:459), Figure 192 (SEQ ID NO:464), Figure 194 (SEQ ID NO:466), Figure 196 (SEQ ID NO:468), Figure 198 (SEQ ID NO:470), Figure 200 (SEQ ID NO:472), Figure 202 (SEQ ID NO:477), Figure 204 (SEQ ID NO:483), Figure 207 (SEQ ID NO:488), Figure 209 (SEQ ID NO:496), Figure 211 (SEQ ID NO:498), Figure 213 (SEQ ID NO:506), Figure 215 (SEQ ID NO:508), Figure 217 (SEQ ID NO:510), Figure 219 (SEQ ID NO:515), Figure 222 (SEQ ID NO:523) and Figure 225 (SEQ ID NO:526).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by the nucleotide deposited under accession number ATCC 209791, ATCC 209786, ATCC 209788, ATCC 209787, ATCC 209789, ATCC 209617, ATCC 209620, ATCC 209616, ATCC 209679, ATCC 209654,

ATCC 209655, ATCC 209656, ATCC 209721, ATCC 209717, ATCC 209716, ATCC 209722, ATCC 209668, ATCC 209670, ATCC 209718, ATCC 209784, ATCC 209703, ATCC 209808, ATCC 209810, ATCC 209699, ATCC 209811, ATCC 209813, ATCC 209705, ATCC 209806, ATCC 209809, ATCC 209805, ATCC 209812, ATCC 209844, ATCC 209847, ATCC 209845, ATCC 209843, ATCC 209846, ATCC 209750, ATCC 209848, ATCC 209851, ATCC 209754, ATCC 209747, ATCC 209861, ATCC 209862, ATCC 209867, ATCC 209879, 5 ATCC 209868, ATCC 209869, ATCC 209775, ATCC 209772, ATCC 209774, ATCC 209777, ATCC 209905, ATCC 209855, ATCC 209910, ATCC 209424, ATCC 209720, ATCC 209714, ATCC 209785, ATCC 209911, ATCC 209669, ATCC 209704, ATCC 209702, ATCC 209701, ATCC 209700, ATCC 209814, ATCC 209715, ATCC 209807, ATCC 209753, ATCC 209749, ATCC 209748, ATCC 209842, ATCC 209849, ATCC 209880, ATCC 209864, ATCC 209882, ATCC 209883, ATCC 209865, ATCC 209866, ATCC 209857, ATCC 209870, 10 ATCC 209859, ATCC 209653, ATCC 209389, ATCC 209386, ATCC 203242, ATCC 203243, ATCC 209783, ATCC 209487 or ATCC 209680.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.

18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.

19. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 5 (SEQ ID NO:8), Figure 6 (SEQ ID NO:9), Figure 7 (SEQ ID NO:10), Figure 12 (SEQ ID NO:29), Figure 13 (SEQ ID NO:30), Figure 16 (SEQ ID NO:37), Figure 17 (SEQ ID NO:38), Figure 18 (SEQ ID NO:39), Figure 31 (SEQ ID NO:75), Figure 64 (SEQ ID NO:170), Figure 71 (SEQ ID NO:191), Figure 96 (SEQ ID NO:265), Figure 99 (SEQ ID NO:271), Figure 100 (SEQ ID NO:272), Figure 101 (SEQ ID NO:273), Figure 102 (SEQ ID NO:274), Figure 103 (SEQ ID NO:275), Figure 104 (SEQ ID NO:276), Figure 105 (SEQ ID NO:277), Figure 106 (SEQ ID NO:278), Figure 107 (SEQ ID NO:279), Figure 110 (SEQ ID NO:285), Figure 111 (SEQ ID NO:286), Figure 112 (SEQ ID NO:287), Figure 113 (SEQ ID NO:288), Figure 114 (SEQ ID NO:289), Figure 115 (SEQ ID NO:290), Figure 116 (SEQ ID NO:291), Figure 123 (SEQ ID NO:304), Figure 126 (SEQ ID NO:310), Figure 127 (SEQ ID NO:311), Figure 130 (SEQ ID NO:323), Figure 133 (SEQ ID NO:331), Figure 30 35

134 (SEQ ID NO:332), Figure 137 (SEQ ID NO:338), Figure 140 (SEQ ID NO:347), Figure 143 (SEQ ID NO:353), Figure 174 (SEQ ID NO:431), Figure 175 (SEQ ID NO:432), Figure 188 (SEQ ID NO:457), Figure 205 (SEQ ID NO:484), Figure 220 (SEQ ID NO:516), Figure 223 (SEQ ID NO:524), Figure 226 (SEQ ID NO:527), Figure 227 (SEQ ID NO:528) and Figure 228 (SEQ ID NO:529).

**FIGURE 1**

CCAGGTCCAACTGCACCTCGGTTCTATCGATTGAATTCCCCGGGGATCCTCTAGAGATCCCT  
CGACCTCGACCCACGCGTCCGCCAAGCTGGCCCTGCACGGCTGCAAGGGAGGCTCCTGTGGA  
CAGGCCAGGCAGGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCTGAGGCCCCAGC  
AAGGGCTAGGGTCCATCTCCAGTCCCAGGACACAGCAGCGGCCACCATGGCCACGCCTGGGC  
TCCAGCAGCATCAGCAGCCCCCAGGACCGGGGGAGGCACAGGTGGCCCCCACCACCCGGAGG  
AGCAGCTCCTGCCCCCTGTCCGGGGGATGACTGATTCTCCTCCGCCAGGCCACCCAGAGGAGA  
AGGCCACCCCGCCTGGAGGCACAGGCCATGAGGGGCTCTCAGGAGGTGCTGCTGATGTGGCT  
TCTGGTGTGAGCAGTGGGCGGCACAGAGCACGCCTACCGGCCCGGCCGTTAGGGTGTGTGCT  
GTCCCGGGCTCACGGGGACCCTGTCTCCGAGTCGTTTCGTGCAGCGTGTGTACCAGCCCTTCC  
TCACCACCTGCGACGGGCACCGGGCCTGCAGCACCTACCGAACCATTTATAGGACCGCCTAC  
CGCCGCAGCCCTGGGCTGGCCCCCTGCCAGGCCTCGCTACGCGTGTGCCCCGGCTGGAAGAG  
GACCAGCGGGCTTCCTGGGGCCTGTGGAGCAGCAATATGCCAGCCGCCATGCCGGAACGGAG  
GGAGCTGTGTCCAGCCTGGCCGCTGCCGCTGCCCTGCAGGATGGCGGGGTGACACTTGCCAG  
TCAGATGTGGATGAATGCAGTGTAGGAGGGGCGGCTGTCCCCAGCGCTGCATCAACACCGC  
CGGCAGTTACTGGTGCCAGTGTGAGGAGGGGCACAGCCTGTCTGCAGACGGTACACTCTGTG  
TGCCCAAGGGAGGGCCCCCAGGGTGGCCCCCAACCCGACAGGAGTGGACAGTGAATGAAG  
GAAGAAGTGCAGAGGCTGCAGTCCAGGGTGGACCTGCTGGAGGAGAAGCTGCAGCTGGTGTCT  
GGCCCCACTGCACAGCCTGGCCTCGCAGGCACTGGAGCATGGGCTCCCGGACCCCGGCAGCC  
TCCTGGTGCATCCTTCCAGCAGCTCGGCCGCATCGACTCCCTGAGCGAGCAGATTTCTTCTC  
CTGGAGGAGCAGCTGGGGTCTGCTCCTGCAAGAAAGACTCGTGACTGCCCAGCGCCCCAGG  
CTGGACTGAGCCCCCTCACGCCGCCCTGCAGCCCCCATGCCCCTGCCCAACATGCTGGGGGTC  
CAGAAGCCACCTCGGGGTGACTGAGCGGAAGGCCAGGCAGGGCCTTCCTCCTTTTCTCCTC  
CCCTTCCCTCGGGAGGGTCCCCAGACCCTGGCATGGGATGGGCTGGGATTTTTTTTGTGAAT  
CCACCCCTGGCTACCCCCACCCTGGTTACCCCAACGGCATCCCAAGGCCAGGTGGGCCCTCA  
GCTGAGGGAAGGTACGAGTTCCCCTGCTGGAGCCTGGGACCCATGGCACAGGCCAGGCAGCC  
CGGAGGCTGGGTGGGGCCTCAGTGGGGGCTGCTGCCTGACCCCCAGCACAATAAAAATGAAA  
CGTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAGGGCGGCCGCGACTCT  
AGAGTCGACCTGCAGAAGCTTGGCCGCCATGGCCCAACTTGTTTATTGCAGCTTATAATGCT  
TACAAAT

**FIGURE 2**

MTDSPPPGHPPEEKATPPGGTGHEGLSGGAADVASGVGSGRHRARLPARPLGCVLSRAHGDPV  
SESFVQRVYQPFLLTTCDGHRACSTYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGAC  
GAAICQPPCRNGGSCVQPGRCRCPAGWRGDTQCSDVDECSARRGGCPQRCINTAGSYWCQCW  
EGHSLSADGTLCPVKGPPRVAPNPTGVDSAMKEEVQRLQSRVDLLEEKQLVLAPLHSLAS  
QALEHGLPDPGSLLVHSFQQLGRIDSLSEQISFLEEQLGSCSCKKDS

**FIGURE 3**

CGCTCGCCCCGTGCCCCCTCGCCTCCCCCGCAGAGTCCCCTCGCGGCAGCAGATGTGTGTGGG  
GTCAGCCACGGCGGGGACTATGGTGAAATTCGCGCGCTCACGCACTACTGGCCCCGTGATC  
CGGTTCTTGGTGCCCCCTGGGCATCACCACATAGCCATCGACTTCGGGGAGCAGGCCTTGAA  
CCGGGGCATTGCTGCTGTCAAGGAGGATGCAGTCGAGATGCTGGCCAGCTACGGGCTGGCGT  
ACTCCCTCATGAAGTTCTTCACGGGTCCCATGAGTGACTTCAAAAATGTGGGCCTGGTGTTT  
GTGAACAGCAAGAGACAGGACCAAAGCCGTCTGTGTATGGTGGTGGCAGGGGCCATCGC  
TGCCGTCTTTCACACACTGATAGCTTATAGTGATTTAGGATACTACATTATCAATAAACTGC  
ACCATGTGGACGAGTCGGTGGGGAGCAAGACGAGAAGGGCCTTCCTGTACCTCGCCGCTTT  
CCTTTCATGGACGCAATGGCATGGACCCATGCTGGCATTCTCTTAAACACAAATACAGTTT  
CCTGGTGGGATGTGCCTCAATCTCAGATGTGATAGCTCAGGTTGTTTTTGTAGCCATTTTGC  
TTCACAGTCACCTGGAATGCCGGGAGCCCCCTGCTCATCCCGATCCTCTCCTGTACATGGGC  
GCACTTGTGCGCTGCACCACCCTGTGCCTGGGCTACTACAAGAACATTACAGCATCATCCC  
TGACAGAAGTGGCCCGGAGCTGGGGGGAGATGCAACAATAAGAAAGATGCTGAGCTTCTGGT  
GGCCTTTGGCTCTAATTCTGGCCACACAGAGAATCAGTCGGCCTATTGTCAACCTCTTTGTT  
TCCCGGACCTTGGTGGCAGTTCTGCAGCCACAGAGGCAGTGGCGATTTTGACAGCCACATA  
CCCTGTGGGTACATGCCATACGGCTGGTTGACGGAAATCCGTGCTGTGTATCCTGCTTTTCG  
ACAAGAATAACCCAGCAACAACTGGTGAGCAGGAGCAACACAGTCACGGCAGCCACATC  
AAGAAGTTTCACTTTCGTCTGCATGGCTCTGTCACTCAGCTCTGTTTTCGTGATGTTTTGGAC  
ACCAACGTGTCTGAGAAAATCTTGATAGACATCATCGGAGTGGACTTTGCCTTTGCAGAAC  
TCTGTGTTGTTCTTTTGCAGTCTTCTCTTCTCCAGTTCAGTCACAGTGAGGGCGCAT  
CTCACCGGTGGCTGATGACACTGAAGAAACCTTCGTCTTGGCCCCAGCTCTGTGCTGCG  
GATCATCGTCTCATCGCCAGCCTCGTGGTCTACCTACCTGGGGGTGCACGGTGCAGCCC  
TGGGCGTGGGCTCCCTCCTGGCGGGCTTTGTGGGAGAATCCACCATGGTTCGCCATCGTGG  
TGCTATGTCTACCGGAAGCAGAAAAGAAGATGGAGAATGAGTCGGCCACGGAGGGGAAGA  
CTCTGCCATGACAGACATGCCTCCGACAGAGGAGGTGACAGACATCGTGGAAATGAGAGAGG  
AGAATGAATAAGGCACGGGACGCCATGGGCACTGCAGGGACGGTCAGTCAGGATGACACTTC  
GGCATCATCTCTCCCTCTCCCATCGTATTTTGTTCCTTTTTTTTGTGTTTTGTTTGGTAAT  
GAAAGAGGCCTTGATTTAAAGGTTTCGTGTCAATTCTCTAGCATACTGGGTATGCTCACACT  
GACGGGGGGACCTAGTGAATGGTCTTTACTGTGCTATGTAAAAACAAACGAAACAACTGAC  
TTCATACCCCTGCCTCACGAAAACCCAAAGACAGCTGCCTCACGGTTGACCTGTGTGTC  
TCCTCCCCGGGACAATCTCCTCTTGGAAACCAAGGACGTCAGCTGTGCCATCGCGCTCGGT  
CACCTGCACAGCAGGCCACAGACTCTCCTGTCCCCCTTCATCGCTCTTAAGAATCAACAGG  
TTAAAACTCGGCTTCCTTTGATTTGCTTCCAGTCACATGGCCGTACAAAGAGATGGAGCCC  
CGGTGGCCTCTTAAATTTCCCTTCTGCCACGGAGTTCGAAACCATCTACTCCACACATGCAG  
GAGGCGGTGGCAGCTGCAGCCCGGAGTCCCCGTTCACTGAGGAACGGAGACCTGTGAC  
CACAGCAGGCTGACAGATGGACAGAATCTCCCGTAGAAAGGTTTGGTTTGAATGCCCCGGG  
GGCAGCAAACCTGACATGGTTGAATGATAGCATTTCACTCTGCGTTCTCCTAGATCTGAGCAA  
GCTGTCAGTTCTACCCCCACCGTGTATATACATGAGCTAACTTTTTTAAATTGTCAAAAA  
GCGCATCTCCAGATTCAGACCCTGCCGCATGACTTTTCTGAAGGCTTGCTTTTCCCTCGC  
CTTTCCTGAAGGTGCGATTAGAGCGAGTCACATGGAGCATCCTAACTTTGCATTTTAGTTTT  
TACAGTGAACCTGAAGCTTTAAGTCTCATCCAGCATCTAATGCCAGGTTGCTGTAGGGTAAC  
TTTTGAAGTAGATATATTACCTGGTTCTGCTACTCTTAGTCATAACTCTGCGGTACAGGTAA  
TTGAGAATGTACTACGGTACTTCCCTCCACACCATAACGATAAAGCAAGACATTTTATAACG  
ATACCAGAGTCACTATGTGGTCTCCCTGAAATAACGCATTTCGAAATCCATGCAGTGCAGTA  
TATTTTTCTAAGTTTTGGAAGCAGGTTTTTCTTTTAAAAAAATTATAGACACGGTTCAGT  
AAATTGATTTAGTCAGAATTCCTAGACTGAAAGAACCTAAACAAAAAAATTTTTAAAGATA  
TAAATATATGCTGTATATGTTATGTAATTTATTTTAGGCTATAATACATTCCTATTTTCGC  
ATTTTCAATAAAATGTCTCTAATAACAAAAA



**FIGURE 4**

MVKFPALTHYWPLIRFLVPLGITNIAIDFGEQALNRGIAAVKEDAVEMLASYGLAYSLMKFF  
TGPMSEDFKNVGLVFVNSKRDRTKAVLCMVVAGAIAAVFHTLIAYSDLGYYIINKLHHVDESV  
GSKTRRAFLYLAAFPFMDAMAWTHAGILLKHKYSFLVGCASISDVIAQVVFVAILLHSHLEC  
REPLLIPILSLYMGALVRCTTLC LGYYKNIHDIIPDRSGPELGGDATIRKMLSFWWPLALIL  
ATQIRISRPVNLVFSRDLGGSSAATEAVAILTATYPVGHMPYGWLTEIRAVYPAFDKNPNPSN  
KLVSTSNVTAAHIKKFTFVCMALSLTLCFVMFWTPNVSEKILIDIIGVDFAFaelcVvPLR  
IFSFFPVPVTVRAHLTGWMLTKKTFVLAPSSVLRIIVLIASLVVLPYLGvHGATLGvGSLl  
AGFVGESTMVAIAACYVYRKQKKMENESATEGEDSAMTDMPPTEEVTDIVEMREENE

**FIGURE 5**

CCTGACAGAAGTGCCCCGGAGCTGGGGGAGATNCAACATTAAGAAGATGCTGAGCTTCTGGT  
GCCNTTTGGCTCTAATTCTGGCCACACAGAGAANCAGTCGGCCTATTGTCAACCTCTTTGTT  
TCCCGGGACCTTGGTGGCAGTTCTGCAGCCACAGAGGCAGTGGCGATTTTGACAGCCACATA  
CCCTGTGGGTACATGCCATACGGCTGGTTGACGGAAATCCGTGCTGTGTATCCTGCTTTTCG  
ACAAGAATAACCCAGCAACAACTGGTGAGCACGAGCAACACAGTCACGGCGGGCCACATC  
AAGAAGTTCACCTTCGTCTGCATGGCTCTGTCACTCACGCTCTGTTTTCGTGATGTTTTGGAC  
ACCCAACGTGTCTGNGAAAATCTTGATAGACATCATCGGAGTGGACTTTGCCTTTGCAGAAC  
TCTGTGTTGTTCCCTTTGCGGATCTTCTCCTTCTTCCAGTTCAGTCACAGTGAGGGCGCAT  
CTCACCGGGTGGCTGATGACACTGAAGAAAACCTTCGTC

**FIGURE 6**

TGACGGAATCCCGGGCTGGGTATCCTGGTTTNGACAAGATAAACCCCCAGCAANAAATTGGG  
GAGCAGGGCAAACAGTNACGGGCAGCCCACATCAAGAAGTTCACCTTNGTTTGNATGGNTC  
TGTCAACTCACGCTNTGTTTCGTGATGTTTTGGACACCCAAAGTGTTTGAGAAAATTTTGAT  
AGACATNATCGGAGTGGANTTTGCCTTTGCAGAANTTTGNGNTGTTCCCTTGC GGATT TTTCT  
CCTTTTTCCCAGTTCCAGTCACAGNGAGGGCGCATCTCACCGGGNGGNTGATGACANTGAAG  
AAAACCTTTGTCCTTGCCCCCAGCTNTTTGGTGCGGATCATTGTCCTNATNGCCAGCCTTGT  
GGTCCTACCCTACCTGGGGGTGCACGGTGCGACCCTGGGCGTGGGTTCCCTCCTGGCGGGCA

**FIGURE 7**

TATTTCCAGTTCCGGTCACGGGGAGGGCGCATNTCACCGGGTGGCTGANGACACTGAAGAAA  
ACCTTNGTCCTTGCCCCCAGNTTTGTGNTGCGGATNATCGTCCTCATCGCCAGCCTNGTGGT  
CCTACCCTACCTGGGGGTGCACGGTGAGAC

**FIGURE 8**

GCCCCGCGCCCGGCGCCGGGCGCCCGAAGCCGGGAGCCACCGCCATGGGGGCCTGCCTGGGA  
GCCTGCTCCCTGCTCAGCTGCGCGTCCTGCCTCTGCGGCTCTGCCCCCTGCATCCTGTGCAG  
CTGCTGCCCCGCCAGCCGCAACTCCACCGTGAGCCGCCTCATCTTCACGTTCTTCCTCTTCC  
TGGGGGTGCTGGTGTCCATCATTATGCTGAGCCCGGGCGTGGAGAGTCAGCTCTACAAGCTG  
CCCTGGGTGTGTGAGGAGGGGGCCGGGATCCCCACCGTCCTGCAGGGCCACATCGACTGTGG  
CTCCCTGCTTGGCTACCGCGCTGTCTACCGCATGTGCTTCGCCACGGCGGCCTTCTTCTTCT  
TCTTTTTTCAACCCTGCTCATGCTCTGCGTGAGCAGCAGCCGGGACCCCCGGGCTGCCATCCAG  
AATGGGTTTTGGTTCTTTAAGTTCCTGATCCTGGTGGGCCTCACCGTGGGTGCCCTTCTACAT  
CCCTGACGGCTCCTTCACCAACATCTGGTTCCTACTTCGGCGTCGTGGGCTCCTTCCTCTTCA  
TCCTCATCCAGCTGGTGTGCTCATCGACTTTGCGCACTCCTGGAACCAGCGGTGGCTGGGC  
AAGGCCGAGGAGTGCGATTCCCGTGCTGGTACGCAGGCCTCTTCTTCTTCACTCTCCTCTT  
CTACTTGCTGTGATCGCGGCCGTGGCGCTGATGTTTATGTACTACACTGAGCCCAGCGGCT  
GCCACGAGGGCAAGGTCTTCATCAGCCTCAACCTCACCTTCTGTGTCTGCGTGTCCATCGCT  
GCTGTCTGCCCCAAGGTCCAGGACGCCCCAGCCCAACTCGGGTCTGCTGCAGGCCTCGGTCTAT  
CACCTCTACACCATGTTTGTACCTGGTCAGCCCTATCCAGTATCCCTGAACAGAAATGCA  
ACCCCCATTTGCCAACCAGCTGGGCAACGAGACAGTTGTGGCAGGCCCCGAGGGCTATGAG  
ACCCAGTGGTGGGATGCCCCGAGCATTGTGGGCCTCATCATCTTCCTCCTGTGCACCTCTT  
CATCAGTCTGCGCTCCTCAGACCACCGGCAGGTGAACAGCCTGATGCAGACCGAGGAGTGCC  
CACCTATGCTAGACGCCACACAGCAGCAGCAGCAGGTGGCAGCCTGTGAGGGCCGGGCC  
TTTGACAACGAGCAGGACGGCGTCACCTACAGCTACTCCTTCTTCCACTTCTGCCTGGTGT  
GGCCTCACTGCACGTCATGATGACGCTCACCAACTGGTACAAGCCCGGTGAGACCCGGAGAG  
TGATCAGCACGTGGACCGCCGTGTGGGTGAAGATCTGTGCCAGCTGGGCAGGGCTGCTCCTC  
TACCTGTGGACCCTGGTAGCCCCACTCCTCCTGCGCAACCGCGACTTCAGCTGAGGCAGCCT  
CACAGCCTGCCATCTGGTGCCTCCTGCCACCTGGTGCCTCTCGGCTCGGTGACAGCCAACCT  
GCCCCCTCCCCACACCAATCAGCCAGGCTGAGCCCCCACCCCTGCCCCAGCTCCAGGACCTG  
CCCCTGAGCCGGGCCTTCTAGTCGTAGTGCTTCAGGGTCCGAGGAGCATCAGGCTCCTGCA  
GAGCCCCATCCCCCGCCACACCCACACGGTGGAGCTGCCTCTTCTTCCCCCTCCTCCCTGT  
TGCCCATACTCAGCATCTCGGATGAAAGGGCTCCCTTGTCTCAGGCTCCACGGGAGCGGGG  
CTGCTGGAGAGAGCGGGGAACCTCCACACAGTGGGGCATCCGGCACTGAAGCCCTGGTGT  
CCTGGTCACGTCCCCAGGGGACCCTGCCCCCTTCTGGACTTCGTGCCTTACTGAGTCTCT  
AAGACTTTTTCTAATAAACAAGCCAGTGCCTGTAAAAAAA

**FIGURE 9**

MGACLGACSLSCASCLCGSAPCILCSCCPASRNSTVSRILFTFFLFLGVLVSIIMLSPGVE  
SOLYKLPWVCEEAGIPTVLQGHIDCGSLLGYRAVYRMCFATAAFFFFFFTLLMLCVSSSRD  
PRAAIQNGFWFFKFLILVGLTVGAFYIPDGSFTNIWFYFGVVGSLFLILIQLVLLIDFAHSW  
NQRWLKGAEEDSRAWYAGLFFFTLLFYLLSIAAVALMFMYYTEPSGCHEGKVFISLNLTFC  
VCVSIAAVLPKVQDAQPNSSGLLQASVITLYTMFVTWSALSSIPEQKCNPHLPTQLGNETVVA  
GPEGYETQWWDAPSIVGLIIFLLCTLFISLRSSDHRQVNSLMQTEECPPMLDATQQQQQQVA  
ACEGRAFDNEQDGVTSYSFFHFCLVLASLHVMMTLTNWYKPGETRKMISTWTAVVVKICAS  
WAGLLLYLWTLVAPLLLRNRDFS

**FIGURE 10**

GAGCGAGGCCGGGACTGAAGGTGTGGGTGTCGAGCCCTCTGGCAGAGGGTTAACCTGGGTC  
AAATGCACGGATTCTCACCTCGTACAGTTACGCTCTCCCGCGGCACGTCCGCGAGGACTTGA  
AGTCCTGAGCGCTCAAGTTTGTCCGTAGGTGAGAGAAGGCCATGGAGGTGCCGCCACCGGC  
ACCGCGGAGCTTTCTCTGTAGAGCATTGTGCCTATTTCCCCGAGTCTTTGCTGCCGAAGCTG  
TGACTGCCGATTTCGGAAGTCCTTGAGGAGCGTCAGAAGCGGCTTCCCTACGTCCCAGAGCCC  
TATTACCCGGAATCTGGATGGGACCGCCTCCGGGAGCTGTTTGGCAAAGATGAACAGCAGAG  
AATTTCAAAGGACCTTGCTAATATCTGTAAGACGGCAGCTACAGCAGGCATCATTGGCTGGG  
TGTATGGGGGAATACCAGCTTTTATTATGCTAAACAACAATACATTGAGCAGAGCCAGGCA  
GAAATTTATCATAACCGGTTTGTATGCTGTGCAATCTGCACATCGTGCTGCCACACGAGGCTT  
CATTGCTTATGGCTGGCGCTGGGGTTGGAGAACTGCAGTGTTTGTGACTATATTCAACACAG  
TGAACACTAGTCTGAATGTATACCGAAATAAAGATGCCTTAAGCCATTTTGTAAATTGCAGGA  
GCTGTACCGGGAAGTCTTTTTTAGGATAAACGTAGGCCTGCGTGGCCTGGTGGCTGGTGGCAT  
AATTGGAGCCTTGCTGGGCACTCCTGTAGGAGGCCTGCTGATGGCATTTCAGAAGTACGCTG  
GTGAGACTGTTTACGAAAGAAAACAGAAGGATCGAAAGGCACTCCATGAGCTAAAACCTGGAA  
GAGTGGAAAGGCAGACTACAAGTTACTGAGCACCTCCCTGAGAAAATTGAAAGTAGTTTACG  
GGAAGATGAACCTGAGAATGATGCTAAGAAAATTGAAGCACTGCTAAACCTTCCTAGAAACC  
CTTCAGTAATAGATAAAACAAGACAAGGACTGAAAGTGCTCTGAACCTTGAAACTCACTGGAGA  
GCTGAAGGGAGCTGCCATGTCCGATGAATGCCAACAGACAGGCCACTCTTTGGTCAGCCTGC  
TGACAAATTTAAGTGCTGGTACCTGTGGTGGCAGTGGCTTGCTCTTGTCTTTTCTTTTCTT  
TTTAACTAAGAATGGGGCTGTTGTACTCTCACTTTACTTATCCTTAAATTTAAATACATACT  
TATGTTTGTAATTAATCTATCAATATATGCAATACATGGATATATCCACCCACCTAGATTTTAA  
GCAGTAAATAAAACATTTTCGCAAAAGATTAAAGTTGAATTTTACAGTTT

**FIGURE 11**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA23318

><subunit 1 of 1, 285 aa, 1 stop

><MW: 32190, pI: 9.03, NX(S/T): 2

MEVPPAPRSFLCRALCLFPRVFAAEAVTADSEVLEERQKRLPYVPEPYYPESGWDRLRELF  
GKDEQQRISKDLANICKTAATAGIIGWVYGGIPAFIHAKQQYIEQSQAETIYHNRFDVQSAH  
RAATRGFIRYGWRWGWRTAVFVTIFNTVNTSLNVYRNKDALSHFVIAGAVTGSLEFRINVGLR  
GLVAGGIIGALLGTPVGGLLMAFQKYAGETVQERKQKDRKALHELEWKGRQLQVTEHLPE  
KIESSLREDEPENDAKKIEALLNLPRNPSVIDKQDKD

**Important Features:****Signal Peptide:**

amino acids 1-24

**Transmembrane domains:**

amino acids 76-96 and amino acids 171-195

**N-glycosylation site:**

amino acids 153-156



**FIGURE 12**

CGGAAGTCCCTTGAGGAGCGTCAGAAGCGGCTTCCCTACGTCCCAGAGCCCTATTACCCGGA  
ATCTGGATGGGACCGCTCCGGGAGCTGTTTGGCAAAGATGAACAGCAGAGAATTTCAAAGGA  
CCTTGCTAATATCTGTAAGACGGCAGCTACAGCAGGCATCATTGGCTGGGTGTATGGGGGAA  
TACCAGCTTTTATTCATGCTAAACAACAATACATTGAGCAGAGCCAGGCAGAAATTTATCAT  
AACCGGTTTGATGCTGTGCAATCTGCACATCGTGCTGCCACACGAGGCTTCATTCGTTTCATG  
GCTGGCGCCGAACC

**FIGURE 13**

TCAAGTTTGTCCGTAGGTCGAGAGAAGGCCATGGAGGTGCCGCCACCGGCACCGCGGAGCTT  
TTTTCTGTAGAGCATTGTGCCTATTTCCCCGAGTTTTTGCTGCCGAAGCTGTGACTGCCGAT  
TCGGAAGTCCTTGAGGAGCGTCAGAAGCGGCTTCCCTACGTCCCAGAGCCCTATTACCCGGA  
ATTTGGATGGGACCGCCTCCGGGAGCTGTTTGGCAAAGATGAACAGCAGAGAATTTCAAAGG  
ACCTTGCTGATATNTGTAAGACGGCAGCTACAGCAGGCATCATTGGCTGGGTGTATGGGGGA  
ATACCAGCTTTTATTCATGNTAAACAACAATACATTGAGCAGAGCCAGGCAGAAATTTATNA  
TAACC



**FIGURE 15**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA39979

><subunit 1 of 1, 204 aa, 1 stop

><MW: 22147, pI: 8.37, NX(S/T): 3

MVCGGFACSKNCLCALNLLYTLVSLLLIGIAAWGIGFGLISSLRVVGVVIAVGIFLEFLIALV  
GLIGAVKHHQVLLFFYMIILLVLFIVQFSVSCACALNQEQQGQLLEVGVNNTASARNDIQR  
NLNCCGFRSVNPNDTCLASCVKSDHSCSPCAPIIGEYAGEVLRVFGGIGLFFSFTEILGVWL  
TYRYRNQKDPRANPSAFL

**Signal Peptide:**

amino acids 1-34

**Transmembrane domains:**

amino acids 47-63, 72-95 and 162-182

**FIGURE 16**

TGATTGGAGCTGTAAAAAANTCTTCAGGTGTTGTNATTTTTTTATATGATTATTCTGTAANT  
TGTATTTATTGTTTCAGTTTTNTGTATCTTGCGCTTGTTTAGCCNTGAACCAGGAGCAACAGG  
GTCAGNTTNTGGAGGTGGTTGGAACAATACGGCAAGTGCTCGAAATGACATCCAGAGAAAT  
NTAAACTGCTGTGGGTCCGAAGTGTTAACCCTGACACCTGTTNTGGCTAGCTGTGTTAA  
AAGTGACCACTNGTGCTCGCCATGTGCTCCAATCATAGGAGAATATGCTGGAGAGGTTTTGA  
GATTTGTTGGTGGCATTGGCCTGTTNTTCAGTTTACAGAGATCCTGGGTGTTTGGCTGACC  
TACAGATACAGGAACCAG

**FIGURE 17**

AATCCCAAATTCCCCAATTTTTTTGGNCTTTTATAGGGAAAGATGTGTTGTGGTAAAAAGTGT  
TAGTATAAAAATGATAATTTACTTGTAGTCTTTTATGATTACACCAATGTATTCTAGAATAG  
TTATGTCTTAGGAAATTGTGGTTTAATTTTTGACTTTTACAGGTAAGTGCAAAGGAGAAGTG  
GTTTCATGAAATGTTCTAATGTATAATAACATTTACCTTCAGCCTCCCATCAGAATGGAACG  
AGTTTTGAGTAATCCAGGAAGTATATCTATATGATCTTGATATTGTTTTATATAATTTGAAG  
TCTAAAAGACTGCATTTTTTAAACAAGTTAGTATTAATGCGTTGGCCACGTAGCAAAAAGAT  
ATTTGATTATCTTAAAAATTGTTAAATACCGTTTTTCATGAAAGTTCTCAGTATTGTAACAGC  
AACTTGTCAAACCTAAGCATATTTGAATATGATCTCCCATATTTGAAATTGAAATCGTATT  
GTGTGGAGGAAATGGCAATCTTATGTGTGCTGAAGGACACAGTAAGAGCACCAAGTTGTGCC  
CCACTTGC

**FIGURE 18**

ATGATTATTCTGTTACTTGTATTTATTGTTTCAGTTTTATGGTATCTTGCGCTTGTTTAGCCC  
CTGAAACCAGGAGCAACAGGGNNCAGCTTCCTGGAGGTTGGTTGGCAACAATCACGGCCAAG  
TGA TCCGCAAATGACATCCCAGAGAAATCCTAACTGCTGTGGGTTCCGAAGTGTTAACCC  
AAATGACACCTGTCTGGCTNGCTGTGTTAAAAGTGACCACTCGTGCTCGCCATGTGCTCCAA  
TCATAGGAGAATATGC

**FIGURE 19**

CAGTCACCAATGAAGCTGGGCTGTGTCCTCATGGCCTGGGCCCTCTACCTTTCCCTTGGTGTG  
CTCTGGGTGGCCAGATGCTACTGGCTGCCAGTTTTGAGACGCTGCAGTGTGAGGGACCTGT  
CTGCACTGAGGAGAGCAGCTGCCACACGGAGGATGACTTGACTGATGCAAGGGAAGCTGGCT  
TCCAGGTCAAGGCCTACACTTTTCAGTGAACCTTCCACCTGATTGTGTCTATGACTGGCTG  
ATCCTCCAAGGTCCAGCCAAGCCAGTTTTTGAAGGGGACCTGCTGGTTCTGCGCTGCCAGGC  
CTGGCAAGACTGGCCACTGACTCAGGTGACCTTCTACCGAGATGGCTCAGCTCTGGGTCCCC  
CCGGGCCTAACAGGGAATTCTCCATCACCGTGGTACAAAAGGCAGACAGCGGGCACTACCAC  
TGCAGTGGCATCTTCCAGAGCCCTGGTCCTGGGATCCCAGAAACAGCATCTGTTGTGGCTAT  
CACAGTCCAAGAACTGTTTCCAGCGCCAATTCTCAGAGCTGTACCCTCAGCTGAACCCCAAG  
CAGGAAGCCCCATGACCTGAGTTGTCAGACAAAGTTGCCCCTGCAGAGGTGAGCTGCCCCG  
CTCCTCTTCTCCTTCTACAAGGATGGAAGGATAGTGCAAAGCAGGGGGCTCTCCTCAGAATT  
CCAGATCCCCACAGCTTCAGAAGATCACTCCGGGTCACTGGTGTGAGGCAGCCACTGAGG  
ACAACCAAGTTTGGAACAGAGCCCCCAGCTAGAGATCAGAGTGCAGGGTGCTTCCAGCTCT  
GCTGCACCTCCACATTGAATCCAGCTCCTCAGAAATCAGCTGCTCCAGGAACTGCTCCTGA  
GGAGGCCCCCTGGGCCTCTGCCTCCGCCGCCAACCCCATCTTCTGAGGATCCAGGCTTTTCTT  
CTCCTCTGGGGATGCCAGATCCTCATCTGTATCACCAGATGGGCCTTCTTCTCAACACATG  
CAGGATGTGAGAGTCCTCCTCGGTACCTGCTCATGGAGTTGAGGGAATTATCTGGCCACCA  
GAAGCCTGGGACCACAAAGGCTACTGCTGAATAGAAAGTAAACAGTTCATCCATGATCTCACT  
TAACCACCCCAATAAATCTGATTCTTTATTTTCTTCTCCTGTCCTGCACATATGCATAAGTA  
CTTTTACAAGTTGTCCCAGTGTTTTGTTAGAATAATGTAGTTAGGTGAGTGTAATAAATTT  
ATATAAAGTGAGAATTAGAGTTTAGCTATAATTGTGTATTCTCTCTTAACACAACAGAAATTC  
TGCTGTCTAGATCAGGAATTTCTATCTGTTATATCGACCAGAATGTTGTGATTTAAAGAGAA  
CTAATGGAAGTGGATTGAATACAGCAGTCTCAACTGGGGGCAATTTTGCCCCCAGAGGACA  
TTGGGCAATGTTTGGAGACATTTTGGTCATTATACTTGGGGGGTTGGGGGATGGTGGGATGT  
GTGTCTACTGGCATCCAGTAAATAGAAGCCAGGGGTGCCGCTAAACATCCTATAATGCACAG  
GGCAGTACCCCAACGAAAAATAATCTGGCCCAAATGTCAGTTGTACTGAGTTTGAGAAA  
CCCCAGCCTAATGAAACCCTAGGTGTTGGGCTCTGGAATGGGACTTTGTCCCTTCTAATTAT  
TATCTCTTCCAGCCTCATTGAGTATTCTTACTGACATACCAGTCTTTAGCTGGTGCTATG  
GTCTGTTCTTTAGTTCTAGTTTGTATCCCCCTCAAAGCCATTATGTTGAAATCCTAATCCCC  
AAGGTGATGGCATTAAAGAAGTGGGCCTTTGGGAAGTGATTAGATCAGGAGTGAGAGCCCTC  
ATGATTAGGATTAGTGCCCTTATTTAAAAAGGCCCCAGAGAGCTAACTCACCTTCCACCAT  
ATGAGGACGTGGCAAGAAGATGACATGTATGAGAACCACAAAAACAGCTGTCGCCAAACACCG  
ACTCTGTCGTTGCCTTGATCTTGAACCTCCAGCCTCCAGAACTATGAGAAATAAATTCTGG  
TTGTTTGTAGCCTAA



**FIGURE 20**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA40594  
><subunit 1 of 1, 359 aa, 1 stop  
><MW: 38899, pI: 5.21, NX(S/T): 0  
MKLGCVLMAWALYLSLGLWVAQMLLAASFETLQCEGPVCTEESCHTEDDLTDAREAGFQV  
KAYTFSEPFHLIVSYDWLILQGPAKPVFEGDLLVLRCAWQDWPLTQVTFYRDGSALGPPGP  
NREFSITVVQKADSGHYHCSGIFQSPGPGIPETASVVAITVQELFPAPILRAVPSAEPQAGS  
PMTLSCQTKLPLQRSAARLLFSFYKDGRIVQSRGLSSEFQIPTASEDHSGSYWCEAATEDNQ  
VWKQSPQLEIRVQGASSAAPTTLNPAPQKSAAPGTAPEEAPGPLPPPPTPSSDPGFSSPL  
GMPDPHLYHQMGLLLKHMQDVRVLLGHLLMELRELSGHQKPGTTKATAE

Leucine zipper pattern sequence:

amino acids 12-33

Protein kinase C phosphorylation site:

amino acids 353-355

**FIGURE 21**

CCCACGCGTCCGCCCACGCGTCCGCCCACGGGTCCGCCCACGCGTCCGGGCCACCAGAAGTT  
TGAGCCTCTTTGGTAGCAGGAGGCTGGAAGAAAGGACAGAAGTAGCTCTGGCTGTGATGGGG  
ATCTTACTGGGCCTGCTACTCCTGGGGCACCTAACAGTGGACACTTATGGCCGTCCCATCCT  
GGAAGTGCCAGAGAGTGTAACAGGACCTTGGAAGGGGATGTGAATCTTCCCTGCACCTATG  
ACCCCTGCAAGGCTACACCCAAGTCTTGGTGAAGTGGCTGGTACAACGTGGCTCAGACCCT  
GTCACCATCTTTCTACGTGACTCTTCTGGAGACCATATCCAGCAGGCAAAGTACCAGGGCCG  
CCTGCATGTGAGCCACAAGGTTCCAGGAGATGTATCCCTCCAATTGAGCACCTGGAGATGG  
ATGACCGGAGCCACTACACGTGTGAAGTCACTGGCAGACTCCTGATGGCAACCAAGTCGTG  
AGAGATAAGATTACTGAGCTCCGTGTCCAGAACTCTCTGTCTCCAAGCCCACAGTGACAAC  
TGGCAGCGGTTATGGCTTACGGTGTCCCGAGGGAATGAGGATTAGCCTTCAATGCCAGGCTC  
GGGTTCTCCTCCCATCAGTTATATTTGGTATAAGCAACAGACTAATAACCAGGAACCCATC  
AAAGTAGCAACCCTAAGTACCTTACTCTTCAAGCCTGCGGTGATAGCCGACTCAGGCTCCTA  
TTTCTGCACTGCCAAGGGCCAGGTTGGCTCTGAGCAGCACAGCGACATTGTGAAGTTTGTGG  
TCAAAGACTCCTCAAAGCTACTCAAGACCAAGACTGAGGCACCTACAACCATGACATACCCC  
TTGAAAGCAACATCTACAGTGAAGCAGTCCTGGGACTGGACCACTGACATGGATGGCTACCT  
TGGAGAGACCAGTGCTGGGCCAGGAAAGAGCCTGCCTGTCTTTGCCATCATCTCATCATCT  
CCTTGTGCTGTATGGTGGTTTTTACCATGGCCTATATCATGCTCTGTGCGGAAGACATCCCAA  
CAAGAGCATGTCTACGAAGCAGCCAGGTAAGAAAGTCTCTCCTCTTCCATTTTGGACCCCGT  
CCCTGCCCTCAATTTTGATTACTGGCAGGAAATGTGGAGGAAGGGGGGTGTGGCACAGACCC  
AATCCTAAGGCCGAGGCCCTTCAAGGTCAGGACATAGCTGCCTTCCCTCTCTCAGGCACCTT  
CTGAGGTTTGGTCTGAAACAAAGGATAATCTAGATCCATCTGCCTTCTGCTTCC  
AGAATCCCTGGGTGGTAGGATCCTGATAATTAATTGGCAAGAATTGAGGCAGAAGGGTGGGA  
AACCAGGACCACAGCCCCAAGTCCCTTCTTATGGGTGGTGGGCTCTTGGGCCATAGGGCACA  
TGCCAGAGAGGCCAACGACTCTGGAGAAACCATGAGGGTGGCCATCTTCGCAAGTGGCTGCT  
CCAGTGATGAGCCAACTTCCAGAATCTGGGCAACAACACTACTCTGATGAGCCCTGCATAGGA  
CAGGAGTACCAGATCATCGCCAGATCAATGGCAACTACGCCCGCTGCTGGACACAGTTCC  
TCTGGATTATGAGTTTCTGGCCACTGAGGGCAAAGTGTCTGTTAAAAATGCCCCATTAGGC  
CAGGATCTGCTGACATAATTGCCTAGTCAGTCCTTGCCTTCTGCATGGCCTTCTTCCCTGCT  
ACCTCTCTTCCCTGGATAGCCCAAAGTGTCCGCCTACCAACACTGGAGCCGCTGGGAGTCACT  
GGCTTTGCCCTGGAATTTGCCAGATGCATCTCAAGTAAGCCAGCTGCTGGATTTGGCTCTGG  
GCCCTTCTAGTATCTCTGCCGGGGGCTTCTGGTACTCCTCTCTAAATACCAGAGGGAAGATG  
CCCATAGCACTAGGACTTGGTCATCATGCCTACAGACACTATTCAACTTTGGCATCTTGCCA  
CCAGAAGACCCGAGGGAGGCTCAGCTCTGCCAGCTCAGAGGACCAGCTATATCCAGGATCAT  
TTCTCTTCTTCAAGGGCCAGACAGCTTTTAATTGAAATTGTTATTTACAGGCCAGGGTTCA  
GTTCTGCTCCTCCACTATAAGTCTAATGTTCTGACTCTCTCCTGGTGTCAATAAATATCTA  
ATCATAACAGC

**FIGURE 22**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45416  
><subunit 1 of 1, 321 aa, 1 stop  
><MW: 35544, pI: 8.51, NX(S/T): 0  
MGILLGLLLLGHLLTVDTYGRPILEVPESVTGPWKGDVNLPCITYDPLQGYTQVLVKWLVQRGS  
DPVTIFLRDSSGDHIQQAKYQGRHLVSHKVPBGDVSLQLSTLEMDDRSHYTCEVTWQTPDGNQ  
VVRDKITELRVQKLSVSKPTVTTGSGYGFTVPQGMRLSLQCQARGSPPISYIWKQQTNNQE  
PIKVATLSTLLEKPAVIADSGSYFCTAKGQVGSEQHSDIVKFVVKDSSKLLKTKTEAPTMT  
YPLKATSTVKQSWDWTDDMDGYLGETSAGPGKSLPVFAIILIIISLCCMVVFTMAYIMLCRKT  
SQQEHVYEAAR

**Glycosaminoglycan attachment site:**

amino acids 149-152

**Transmembrane domain:**

amino acids 276-306

**FIGURE 23**

GCGCCGGGAGCCCATCTGCCCCCAGGGGACGGGGCGCGGGGCCGGCTCCCGCCCGGCACAT  
GGCTGCAGCCACCTCGCGCGCACCCGAGGCGCGCGCCAGCTCGCCCGAGGTCCGTGCGA  
GGCGCCCGGCCCGGAGCCAAGCAGCAACTGAGCGGGGAAGCGCCCGGTCCGGGGATC  
GGGATGTCCCTCCTCCTCTCTGCTAGTTTCTACTATGTTGGAACCTTGGGGACTCA  
CACTGAGATCAAGAGAGTGGCAGAGGAAAAGGTCACTTTGCCCTGCCACCATCAACTGGGGC  
TTCCAGAAAAAGACACTCTGGATATTGAATGGCTGCTCACCATAATGAAGGGAACCAAAAA  
GTGGTGATCACTTACTCCAGTCGTCTGTCTACAATAACTTGACTGAGGAACAGAAGGGCCG  
AGTGGCCTTTGCTTCCAATTTCTGGCAGGAGATGCCTCCTTGAGATTGAACCTCTGAAGC  
CCAGTGATGAGGGCCGGTACACCTGTAAGGTTAAGAATTGAGGGCGCTACGTGTGGAGCCAT  
GTCATCTTAAAAGTCTTAGTGAGACCATCCAAGCCCAAGTGTGAGTTGGAAGGAGAGCTGAC  
AGAAGGAAGTGACCTGACTTTGAGTGAGTCACTCTGTCAGAGAGCCCATTTGTGTATT  
ACTGGCAGCGAATCCGAGAGAAAGAGGGAGAGGATGAACGTCTGCCTCCCAAATCTAGGATT  
GACTACAACCACCCTGGACGAGTTCTGCTGCAGAATCTTACCATGTCCTACTCTGGACTGTA  
CCAGTGCACAGCAGGCAACGAAGCTGGGAAGGAAAGCTGTGTGGTGCGAGTAACTGTACAGT  
ATGTACAAAGCATCGGCATGGTTGCAGGAGCAGTGACAGGCATAGTGGCTGGAGCCCTGCTG  
ATTTTCTCTTGGTGTGGCTGCTAATCCGAAGGAAAGACAAAGAAAGATATGAGGAAGAAGA  
GAGACCTAATGAAATTGAGAAAGATGCTGAAGCTCCAAAGCCCGTCTTGTGAAACCCAGCT  
CCTCTTCTCAGGCTCTCGGAGCTCAGCTCTGGTTCTTCTCCTCCACTCGCTCCACAGCAAT  
AGTGCCTCACGCAGCCAGCGGACACTGTCAACTGACGCAGCACCCAGCCAGGGCTGGCCAC  
CCAGGCATACAGCCTAGTGGGGCCAGAGGTGAGAGGTTCTGAACCAAAGAAAGTCCACCATG  
CTAATCTGACCAAAGCAGAAACCACACCCAGCATGATCCCCAGCCAGAGCAGAGCCTTCCAA  
ACGGTCTGAATTACAATGGACTTGACTCCACGCTTTCTTAGGAGTCAGGGTCTTTGGACTC  
TTCTCGTCATTGGAGCTCAAGTCACAGCCACACAACCAGATGAGAGGTCATCTAAGTAGCA  
GTGAGCATTGCACGGAACAGATTGAGATGAGCATTCTTCTTATACAATACCAACAAGCAAA  
AGGATGTAAGCTGATTCTATCTGTAAAAAGGCATCTTATTGTGCCTTTAGACCAGAGTAAGGG  
AAAGCAGGAGTCCAAATCTATTGTGTTGACCAGGACCTGTGGTGAGAAGGTTGGGGAAAGGTG  
AGGTGAATATACCTAAAACCTTTAATGTGGGATATTTTGTATCAGTGCTTTGATTACAAATT  
TTCAAGAGGAAATGGGATGCTGTTTGTAAATTTCTATGCATTTCTGCAAACTTATTGGATT  
ATTAGTTATTGAGACAGTCAAGCAGAACCCACAGCCTTATTACACCTGTCTACACCATGTAC  
TGAGCTAACCACTTCTAAGAAACTCCAAAAAGGAAACATGTGTCTTCTATTCTGACTTAAC  
TTCATTTGTCTAAGGTTTGGATATTAATTTCAAGGGGAGTTGAAATAGTGGGAGATGGAGA  
AGAGTGAATGAGTTTCTCCACTCTATACTAATCTCACTATTTGTATTGAGCCCAAAATAAC  
TATGAAAGGAGACAAAATTTGTGACAAAGGATTGTGAAGAGCTTTCCATCTTCATGATGTT  
ATGAGGATTGTTGACAAACATTAGAAATATATAATGGAGCAATTGTGGATTCCCCCTCAAAT  
CAGATGCCTCTAAGGACTTTCTGCTAGATATTTCTGGAAGGAGAAAATACAACATGTCATT  
TATCAACGTCCTTAGAAAGAATTCTTCTAGAGAAAAAGGGATCTAGGAATGCTGAAAGATTA  
CCCAACATACCATTATAGTCTCTTCTTTCTGAGAAAATGTGAAACCAGAATTGCAAGACTGG  
GTGGACTAGAAAGGGAGATTAGATCAGTTTTCTCTTAATATGTCAAGGAAGGTAGCCGGGCA  
TGGTGCCAGGCACCTGTAGGAAAAATCCAGCAGGTGGAGGTTGCAGTGAGCCGAGATTATGCC  
ATTGCACTCCAGCTGGGTGACAGAGCGGGACTCCGTCTC

**FIGURE 24**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45419  
><subunit 1 of 1, 373 aa, 1 stop  
><MW: 41281, pI: 8.33, NX(S/T): 3  
MSLLLLLLLLVSYVGTLGTHTEIKRVAEEKVTLPCHHQLGLPEKDTLDIEWLLTDNEGNQKV  
VITYSSRHVYNNLTEEQGRVAFASNFLAGDASLQIEPLKPSDEGRYTCKVKNSGRYVWSHV  
ILKVLVRPSKPKCELEGELTEGSDLTQCESSSGTEPIVYYWQRIREKEGEDERLPPKSRID  
YNHPGRVLLQNLTMSYSGLYQCTAGNEAGKESCVVRVTVQYVQSIGMVAGAVTGIVAGALLI  
FLLVWLLIRRKDKERYEEEEERPNEIREDAEAPKARLVKPSSSSSGSRSSRSGSSSTRSTANS  
ASRSQRTLSTDAAPQPGLATQAYSLVGPEVRGSEPKKVHHANLTKAETTPSMIPSQSRAFQTV

Transmembrane domain:

amino acids 221-254

**FIGURE 25**

GTCGTTCCCTTTGCTCTCTCGCGCCAGTCCTCCTCCCTGGTTCTCCTCAGCCGCTGTGGAG  
GAGAGCACCCGGAGACGCGGGCTGCAGTCGCGGGCGGCTTCTCCCCGCTGGGCGGCCTCGCC  
GCTGGGCAGGTGCTGAGCGCCCCCTAGAGCCTCCCTTGCCGCTCCCTCCTCTGCCCGGCCG  
AGCAGTGACATGGGGTGTGGAGGTAGATGGGCTCCCGCCCCGGGAGGCGGCGGTGGATGC  
GGCGCTGGGCAGAACAGCCGCGGATTCCAGCTGCCCCGCGCGCCCCGGGCGCCCCCTGCGAG  
TCCCCGGTTTCAGCCATGGGGACCTCTCCGAGCAGCAGCACCCGCCCTCGCCTCCTGCAGCCGC  
ATCGCCCCGCGGAGCCACAGCCACGATGATCGCGGGCTCCCTTCTCCTGCTTGGATTCTTAG  
CACCACCACAGCTCAGCCAGAAGAGGCTCGAATCTCATTGGCACATACCGCCATGTTG  
ACCGTGCCACCGGCCAGGTGCTAACCTGTGACAAGTGTCCAGCAGGAACCTATGTCTCTGAG  
CATTGTACCAACACAAGCCTGCGCGTCTGCAGCAGTTGCCCTGTGGGGACCTTTACCAGGCA  
TGAGAATGGCATAGAGAAATGCCATGACTGTAGTCAGCCATGCCCATGGCCAATGTTGAGA  
AATTACCTTGTGCTGCCTTGACTGACCGAGAATGCACCTGCCCACCTGGCATGTTCCAGTCT  
AACGCTACCTGTGCCCCCATAACGGTGTGCTCTGTGGGTGGGGTGTGCGGAAGAAAGGGAC  
AGAGACTGAGGATGTGCGGTGTAAGCAGTGTGCTCGGGGTACCTTCTCAGATGTGCCTTCTA  
GTGTGATGAAATGCAAAGCATAACAGACTGTCTGAGTCAGAACCTGGTGGTGATCAAGCCG  
GGGACCAAGGAGACAGACAACGTCTGTGGCACACTCCCGTCTTCTCCAGCTCCACCTCACC  
TTCCCTTGGCACAGCCATCTTTCCACGCCCTGAGCACATGGAAACCCATGAAGTCCCTTCT  
CCACTTATGTTCCCAAAGGCATGAATCAACAGAATCCAACTCTTCTGCCTCTGTTAGACCA  
AAGGTACTGAGTAGCATCCAGGAAGGGACAGTCCCTGACAACACAAGCTCAGCAAGGGGGAA  
GGAAGACGTGAACAAGACCTCCCAAACCTTCAGGTAGTCAACCACCAGCAAGGCCCCACC  
ACAGACACATCCTGAAGCTGCTGCCGTCCATGGAGGCCACTGGGGCGAGAAGTCCAGCACG  
CCCATCAAGGGCCCCAAGAGGGGACATCCTAGACAGAACCTACACAAGCATTGTGACATCA  
TGAGCATTGCCCCGGATGATTGTGCTTTTCTGCTGCTGGTGCTTGTGGTGATTGTGGTGT  
GCAGTATCCGGAAGAGCTCGAGGACTCTGAAAAGGGGGCCCCCGGCAGGATCCAGTGCCATT  
GTGGAAGAGGCAGGGCTGAAGAAATCCATGACTCCAACCCAGAACCGGGAGAAATGGATCTA  
CTACTGCAATGGCCATGGTATCGATATCCTGAAGCTTGTAGCAGCCCAAGTGGGAAGCCAGT  
GGAAAGATATCTATCAGTTTCTTTGCAATGCCAGTGAGAGGGAGGTTGCTGCTTCTCCAAT  
GGGTACACAGCCGACGAGCGGGCTACGCAGCTCTGCAGCACTGGACCATCCGGGGCCCC  
CGAGGCCAGCCTCGCCAGCTAATTAGCGCCCTGCGCCAGCACCGGAGAAACGATGTTGTGG  
AGAAGATTCTGGGCTGATGGAAGACACCCAGCTGGAAGTGAACAACTACCTCTCCCG  
ATGAGCCCGAGCCCGCTTAGCCCGAGCCCCCTCCCGAGCCCCAACCGGAACTTGAGAAATC  
CGCTCTCCTGACGGTGGAGCCTTCCCCACAGGACAAGAACAGGGCTTCTTCTGGATGAGT  
CGGAGCCCCCTTCTCCGCTGTGACTCTACATCCAGCGGCTCCTCCGCGCTGAGCAGGAACGGT  
TCCTTTATTACCAAAGAAAAGAAGGACACAGTGTTGCGGCAGGTACGCCCTGGACCCCTGTGA  
CTTGACGCTATCTTTGATGACATGCTCCACTTTCTAAATCCTGAGGAGCTGCGGGTGATTG  
AAGAGATTCCCCAGGCTGAGGACAACTAGACCGGCTATTGAAATTATTGGAGTCAAGAGC  
CAGGAAGCCAGCCAGACCTCCTGGACTCTGTTTATAGCCATCTTCTGACCTGCTGTAGAA  
CATAGGGATACGATTCTGGAAATTAATCAATTTAGTGGCAGGGTGGTTTTTTAATTTTCT  
TCTGTTTTCTGATTTTGTGTTTGGGGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGTGT  
GTGTGTGTGTGTGTGTTTAAACAGAGAATAGCCAGTGCTTGAGTTCTTTCTCCTTCTCTCT  
CTCTTTTTTTTTTAAATAACTCTTCTGGGAAGTTGGTTTATAAGCCTTGGCAGGTGTAAT  
GTTGTGAAATACCCACCCTAAAGTTTTTTTAAAGTTCCATATTTTCTCCATTTTGCTTCTTA  
TGTATTTTCAAGATTATTCTGTGCACCTTAAATTTACTTAACTTACCATAAATGCAGTGTGA  
CTTTTCCACACACTGGATTGTGAGGCTCTTAACTTCTTAAAGTATAATGGCATCTGTGA  
ATCCTATAAGCAGTCTTTATGTCTCTTAAACATTACACCTACTTTTTTAAAAACAAATATTAT  
TACTATTTTATTATTGTTTGTCTTTATAAATTTTCTTAAAGATTAAAGAAATTTAAGACC  
CCATTGAGTTACTGTAATGCAATTCACCTTTGAGTTATCTTTTAAATATGTCTTGTATAGTT  
CATATTATGCTGAACTTGACCACACTATTGCTGATTGTATGGTTTTTACCTGGACACCG  
TGTAAGTCTTGATTACTTGTACTCTTCTTATGCTAATATGCTCTGGGCTGGAGAAATGAA  
ATCCTCAAGCCATCAGGATTGCTATTTAAGTGGCTTGACAACCTGGGCCACCAAGAACTTG  
AACTTACCTTTTAGGATTTGAGCTGTTCTGGAACACATTGCTGCACTTTGGAAAGTCAAAA  
TCAAGTGCCAGTGGCGCCCTTTCCATAGAGAATTTGCCAGCTTTGCTTTAAAGATGTCTT  
GTTTTTTATATACATAATCAATAGGTCCAATCTGCTCTCAAGGCCTTGGTCTGTGATATAT  
TTCCTTACCAATTACTTTAATTAATAATGGCTGCAACTGTAAGAACCCTTGTCTGATATAT  
TTGCAACTATGCTCCCATTTACAAATGTACCTTCTAATGCTCAGTTGCCAGTTTCCAATGCA  
AAGGTGGCGTGGACTCCCTTTGTGTGGGTGGGGTTTGTGGGTAGTGGTGAAGGACCGATATC  
AGAAAAATGCCTTCAAGTGTACTAATTTATTAATAAACATTAGGTGTTTGTAAAAA



**FIGURE 27**

ATGGGAAGCCAGTAACACTGTGGCCTACTATCTCTTCCGTGGTGCCATCTACATTTTGGGA  
CTCGGGAATTATGAGGTAGAGGTGGAGGCGGAGCCGGATGTCAGAGGTCTGAAATAGTCAC  
CATGGGGGAAAATGATCCGCCTGCTGTTGAAGCCCCCTTCTCATTCCGATCGCTTTTGGCC  
TTGATGATTTGAAAATAAGTCCTGTTGCACCAGATGCAGATGCTGTTGCTGCACAGATCCTG  
TCACTGCTGCCATTGAAGTTTTTCCAATCATCGTCATTGGGATCATTGCATTGATATTAGC  
ACTGGCCATTGGTCTGGGCATCCACTTCGACTGCTCAGGGAAGTACAGATGTCGCTCATCCT  
TTAAGTGTATCGAGCTGATAGCTCGATGTGACGGAGTCTCGGATTGCAAAGACGGGGAGGAC  
GAGTACCGCTGTGTCCGGGTGGGTGAGTCAAGATGCCGTGCTCCAGGTGTTACAGCTGCTTC  
GTGGAAGACCATGTGTCCGATGACTGGAAGGCTACTACGCAAATGTTGCCCTGTGCCCAAC  
TGGGTTTTCCAAGCTATGTGAGTTCAGATAACCTCAGAGTGAGCTCGCTGGAGGGGAGTTT  
CGGGAGGAGTTTGTGTCCATCGATCACCTCTTGCCAGATGACAAGGTGACTGCATTACACCA  
CTCAGTATATGTGAGGGAGGGATGTGCCTCTGGCCACGTGGTTACCTTGCACTGCACAGCCT  
GTGGTCATAGAAGGGGCTACAGCTCACGCATCGTGGGTGGAAACATGTCTTGTCTCTCGCAG  
TGGCCCTGGCAGGCCAGCCTTCAGTTCAGGGCTACCACCTGTGCGGGGGCTCTGTATCAC  
GCCCCGTGTGGATCATCACTGCTGCACACTGTGTTTATGACTTGTACCTCCCCAAGTCATGGA  
CCATCCAGGTGGGTCTAGTTTTCCCTGTTGGACAATCCAGCCCCATCCCACTTGGTGGAGAAG  
ATTGTCTACCACAGCAAGTACAAGCCAAAGAGGCTGGGCAATGACATCGCCCTTATGAAGCT  
GGCCGGCCACTCACGTTCAATGAAATGATCCAGCCTGTGTGCCTGCCCAACTCTGAAGAGA  
ACTTCCCCGAGGAAAAGTGTGCTGGACGTGAGGATGGGGGGCCACAGAGGATGGAGGTGAC  
GCCTCCCCTGTCTGAACCACGCGGCGTCCCTTTGATTTCCAACAAGATCTGCAACCACAG  
GGACGTGTACGGTGGCATCATCTCCCCCTCCATGCTCTGCGCGGGCTACCTGACGGGTGGCG  
TGGACAGCTGCCAGGGGGACAGCGGGGGGCCCTGGTGTGTCAAGAGAGGAGGCTGTGGAAG  
TTAGTGGGAGCGACCAGCTTTGGCATCGGCTGCGCAGAGGTGAACAAGCCTGGGGTGTACAC  
CCGTGTCACCTCCTTCTGACTGGATCCACGAGCAGATGGAGAGAGACCTAAAAACCTGAA  
GAGGAAGGGGACAAGTAGCCACCTGAGTTCCTGAGGTGATGAAGACAGCCCGATCCTCCCCCT  
GGAATCCCGTGTAGGAACCTGCACACGAGCAGACACCCTTGGAGCTCTGAGTTCGGGCACCA  
GTAGCAGGCCCCGAAAGAGGCACCCTTCCATCTGATTCCAGCACAACCTTCAAGCTGCTTTTT  
GTTTTTTGTTTTTTTGGAGGTGGAGTCTCGCTCTGTTGCCAGGCTGGAGTGCAGTGGCGAAA  
TCCCTGCTCACTGCAGCCTCCGCTTCCCTGGTTCAAGCGATTCTCTTGCCTCAGCTTCCCCA  
GTAGCTGGGACCACAGGTGCCCGCCACCACCCCACTAATTTTTCTATTTTTAGTAGAGAC  
AGGGTTTACCATGTTGGCCAGGCTGCTCTCAAACCCCTGACCTCAATGATGTGCTGCTT  
CAGCCTCCCACAGTGCTGGGATTACAGGCATGGGCCACCACGCCTAGCCTCACGCTCCTTTC  
TGATCTTCACTAAGAACAAAAGAAGCAGCAACTTGCAAGGGCGGCCTTTCCCACTGGTCCAT  
CTGGTTTTCTCTCAGGGTCTTGCAAAATTCCTGACGAGATAAGCAGTTATGTGACCTCAG  
TGCAAAGCCACCAACAGCCACTCAGAAAAGACGCACCAGCCAGAAAGTGCAGAACTGCAGTC  
ACTGCACGTTTTTCATCTTAGGGACCAGAACCAACCCACCCTTTCTACTTCCAAGACTTAT  
TTTACATGTGGGGAGGTTAATCTAGGAATGACTCGTTTAAGGCCTATTTTCATGATTTCTT  
TGTAGCATTTGGTGCTTGACGTATTATTGTCCTTTGATTCCAAATAATATGTTTCTTCCCT  
CATTTGTCTGGCGTGTCTGCGTGGACTGGTGACGTGAATCAAATCATCCACTGAAA



**FIGURE 28**

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45234
><subunit 1 of 1, 453 aa, 1 stop
><MW: 49334, pI: 6.32, NX(S/T): 1
MGENDPPAVEAPFSFRSLFGLDDLKISPVAPDADAVAAQILSLLPLKFFPIIVIGIILILA
LAIGLGIHFDCSGKYRCRSSFKCIELIARCDGVSDCKDGEDEYRCVRVGGQNAVQLQVFTAAS
WKTMCSDDWKGHYANVACAQLGFPSYVSSDNLRVSSLEGQFREEFVSIDHLLPDDKV TALHH
SVYVREGCASGHVVTLOCTACGHRRGYSSRIVGGNMSLLSQWPWQASLQFQGYHLCGGSVIT
PLWIIITAHCVDLYLPKSWTIQVGLVSLLDNPAPSHLVEKIVYHISKYKPKRLGNDIALMKL
AGPLTFNEMIQPVCLPNSEENFPDGKVCWTSGWGATEDGGDASPVLNHAAPPLISNKICNHR
DVGGGIISPSMLCAGYLTGGVDSCQGDSSGGLVCQERRLWKLVGATSF GIGCAEVNKP G VYT
RVTSFLDWIHEQMERDLKT
```

**FIGURE 29**

CCCACGCGTCCGTCCTAGTCCCCGGGCCAACTCGGACAGTTTGCTCATTTATTGCAACGGTC  
AAGGCTGGCTTGTGCCAGAACGGCGCGCGCGCGCACGCACACACACGGGGGAAAC  
TTTTTTAAAAATGAAAGGCTAGAAGAGCTCAGCGGCGCGCGCGCGCTGCGCGAGGGCTCCG  
GAGCTGACTCGCCGAGGCAGGAAATCCCTCCGGTTCGCGACGCCCGCGCCCGGCTCGGCGCCC  
GCGTGGGATGGTGCAGCGCTCGCCGCCGGGCCCCGAGAGCTGCTGCACTGAAGGCCGGCGACG  
ATGGCAGCGCGCCCGCTGCCCGTGTCCCCCGCCCGCGCCCTCCTGCTCGCCCTGGCCGGTGC  
TCTGCTCGCGCCCTGCGAGGCCCGAGGGGTGAGCTTATGGAACCAAGGAAGAGCTGATGAAG  
TTGTCACTGCCTCTGTTTCGGAGTGGGGACCTCTGGATCCAGTGAAGAGCTTCGACTCCAAG  
AATCATCCAGAAGTGCTGAATATTCGACTACAACGGGAAAGCAAAGAACTGATCATAAATCT  
GGAAAGAAATGAAGGTCTCATTGCCAGCAGTTTCACGGAAACCCACTATCTGCAAGACGGTA  
CTGATGTCTCCCTCGCTCGAAATTACACGGGTCACTGTTACTACCATGGACATGTACGGGGA  
TATTCTGATTCAAGCAGTCAGTCTCAGCACGTGTTCTGGTCTCAGGGGACTTATTGTGTTGA  
AAATGAAAGCTATGTCTTAGAACCAATGAAAGTGCAACCAACAGATACAAACTCTTCCAG  
CGAAGAAGCTGAAAAGCGTCCGGGGATCATGTGGATCACATCACACACACCAAACCTCGCT  
GCAAAGAATGTGTTTCCACCACCTCTCAGACATGGGCAAGAAGGCATAAAAGAGAGACCT  
CAAGGCAACTAAGTATGTGGAGCTGGTGATCGTGGCAGACAACCGAGAGTTTCAGAGGCAAG  
GAAAAGATCTGGAAGAAAGTTAAGCAGCGATTAAATAGAGATTGCTAATCACGTTGACAAGTTT  
TACAGACCACTGAACATTCCGATCGTGTTGGTAGGCGTGGAAGTGGAATGACATGGACAA  
ATGCTCTGTAAGTCAGGACCCATTACCAGCTCCATGAATTTCTGGACTGGAGGAAGATGA  
AGCTTCTACCTCGCAAATCCCATGACAAATGCGCAGCTTGTCACTGGGGTTTATTTCGAAGG  
ACCACCATCGGCATGGCCCCAATCATGAGCATGTGCACGGCAGACCACTGCGGGGAATTGT  
CATGGACCATTCAGACAATCCCTTGGTGCAGCCGTGACCCTGGCACATGAGCTGGGCCACA  
ATTTCCGGGATGAATCATGACACACTGGACAGGGGCTGTAGCTGTCAAATGGCGGTTGAGAAA  
GGAGGCTGCATCATGAACGCTTCCACCGGGTACCCATTTCCCATGGTGTTCAGCAGTTGCAG  
CAGGAAGGACTTGGAGACCAGCCTGGAGAAAGGAATGGGGGTGTGCCTGTTTAACTGCCGG  
AAGTCAGGGAGTCTTTCGGGGGCCAGAAAGTGTTGGGAACAGATTTGTGGAAGAAGGAGAGGAG  
TGTGACTGTGGGGAGCCAGAGGAATGTATGAATCGCTGCTGCAATGCCACCACCTGTACCCT  
GAAGCCGAGCGCTGTGTGCGCACATGGGCTGTGCTGTGAAGACTGCCAGCTGAAGCCTGCAG  
GAACAGCGTGCAGGGACTCCAGCAACTCCTGTGACCTCCAGAGTTCTGCACAGGGGCCAGC  
CCTCACTGCCAGCCAATGTGTACCTGCACGATGGGCACTCATGTCAAGATGTCCAGGGCTA  
GTGCTACAATGGCATCTGCCAGACTCACGAGCAGCAGTGTGTCAAGCTCTGGGGACCAAGTG  
CTAAACCTGCCCCCTGGGATCTGCTTTGAGAGAGTCAATTTCTGCAGGTGATCCTTATGGCAAC  
TGTGGCAAAGTCTCGAAGAGTTCCTTTGCCAAATGCGAGATGAGAGATGCTAAATGTGGA  
AATCCAGTGTCAAGGAGGTGCCAGCCGGCCAGTCATTGGTACCAATGCCGTTTCCATAGAAA  
CAAACATCCCTCTGCAGCAAGGAGGCCGGATTCTGTGCCGGGGGACCCAGTGTACTTGGGC  
GATGACATGCCGGACCCAGGGCTTGTGCTTGCAGGCACAAAGTGTGCAGATGGAAAAATCTG  
CCTGAATCGTCAATGTCAAAATATTAGTGTCTTTGGGGTTCACGAGTGTGCAATGCAGTGCC  
ACGGCAGAGGGGTGTGCAACAACAGGAAGAACTGCCACTGCGAGGCCCACTGGGCACCTCCC  
TTCTGTGACAAGTTTGGCTTTGGAGGAAGCACAGACAGCGGCCCATCCGGCAAGCAGAAGC  
AAGGCAGGAAGCTGCAGAGTCCAACAGGAGCGCGGCCAGGGCCAGGAGCCCGTGGGATCGC  
AGGAGCATGCGTCTACTGCCTCACTGACATCTGAGCCCTCCCATGACATGGAGACCGT  
GACCAGTGCTGCTGCAGAGGAGTCAAGCGTCCCCAAGGCCTCCTGTGACTGGCAGCATGTA  
CTCTGTGGCTTTGCCATCGTTTCCATGACAACAGACACAACAGTTCTCGGGGCTCAGGAG  
GGGAAGTCCAGCCTACCAGGCACGTCTGCAGAAACAGTGAAGGAAGGGCAGCGACTTCTG  
GTTGAGCTTCTGCTAAAACATGGACATGCTTCAGTGCTGCTCCTGAGAGAGTAGCAGGTTAC  
CACTCTGGCAGGCCCCAGCCCTGCAGCAAGGAGGAAGAGGACTCAAAGTCTGGCCTTTCAC  
TGAGCCTCCACAGCAGTGGGGGAGAAGCAAGGTTGGGGCCAGTGTCCCCTTCCCCAGTGA  
CACCTCAGCCTTGGCAGCCCTGATGACTGGTCTCTGGCTGCAACTTAATGCTCTGATATGGC  
TTTTAGCATTTATTATATGAAAATAGCAGGGTTTTAGTTTTTAATTTATCAGAGACCTGCC  
ACCATTTCCATCTCCATCCAAGCAAAGTGAATGGCAATGAAACAACTGGAGAAGAAGGTAG  
GAGAAAGGGCGGTGAACCTCTGGCTTTTGCTGTGGACATGCGTGACCAGCAGTACTCAGGTT  
TGAGGGTTTGCAGAAAGCCAGGGAACCAAGAGTCACCAACCTTCATTTAACAAGTAAGA  
ATGTTAAAAAGTGAACAATGTAAAGAGCCTAACTCCATCCCCGTGGCCATTACTGCATAA  
AATAGAGTGCATTTGAAAT

**FIGURE 30**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA49624  
><subunit 1 of 1, 735 aa, 1 stop  
><MW: 80177, pI: 7.08, NX(S/T): 5  
MAARPLPVSPARALLLALAGALLAPCEARGVSLWNQGRADEVVVSASVRSGDLWIPVKSFDSK  
NHPEVLNIRLQRESKELIINLERNEGLIASSFTETHYLQDGTDVSLARNYTGHCYYHGHVRG  
YSDSAVSLSTCSGLRGLIVFENESYVLEPMKSATNRYKLFPAKKLKSVRGSCGSHHNTPNLA  
AKNVFPFPSQTWARRHKRETLKATKYVELVIVADNREFQRQGDLEKVKQRLIEIANHVDKF  
YRPLNIRIVLVGVEVWNDMDKCSVSQDPFTSLHEFLDWRKMKLLPRKSHDNAQLVSGVYFQG  
TTIGMAPIMSMCTADQSGGIVMDHSDNPLGAAVTLAHELGHNFGMNHDTLDRGCSCQMAVEK  
GGCIMNASTGYPPFMVFSSCSRKDLETSLEKGMGVCLFNLPEVRESFGGQKCGNRFVEEGEE  
CDCGEPEECMNRCNATTCTLKPDCAHGLCCEDCQLKPAGTACRDSSNSCDLPEFCTGAS  
PHCPANVYLHDGHSCQDVDGYCYNGICQTHEQQCVTLWGPGAKPAPGICFERVNSAGDPYGN  
CGKVS KSSFAKCEMRDAKCGKIQCGGASRPVIGTNAVSIETNIPLQQGGRILCRGTHVYLG  
DDMPDPGLVLAGTKCADGKICLNRCQNISVFGVHECAMQCHGRGVCNNRKNCHCEAHWAPP  
FCDKFGFGGSTDSGPIRQAEARQEAAESNRERGQGQEPVGSQEHASTASLTLI

**FIGURE 31**

TCCCAAGGCTTCTTGGATGGCAGATGATTNTGGGGTTTTGCATTGTTTCCCTGACAACGAAA  
ACAAAACAGTTTTTGGGGGTTTCAGGAGGGGAANTCCAGCCTACCCAGGAAGTTTGCAGAAACA  
GTGCAAGGAAGGGCAGGANTTCCTGGTTGAGNTTTTTGNTAAAACATGGACATGNTTCAGTG  
CTGCTCNTGAGAGAGTAGCAGGTTACCACTTTTGGCAGGCCCCAGCCCTGCAGCAAGGAGGA  
AGAGGACTCAAAAGTTTGGCCTTTCACTGAGCCTCCACAGCAGTGGGGGAGAAGCAAGGGTT  
GGGCCAGTGTCCCCTTTCCCCAGTGACACCTCAGCCTTGGCAGCCCTGATAACTGGTNTNT  
GGCTGCAANTTAATGCTNTGATATGGCTTTTAGCATTTATTATATGAAAATAGCAGGGTTTT  
AGTTTTTAATTTATCAGAGACCCTGCCACCCATTCCATNTCCATCCAAG

**FIGURE 32**

CATCCTGCAACATGGTGAAACCACGCCTGGCTAATTTTGTGTATTTTGGTAGAGATGGGA  
TTTCACCGTGTTAGCCAGGATTGTCTCAATCTGACCTCATGATCTGCCCGCCTCGGCCTCCC  
AAAGTGCTGGGATTACAGGCGAGTGCAACCACACCCGGCCACAACTTTTTAAGAAGTTAAT  
GAAACCATACTTTTACATTTTAAATGACAGGAAAATGCTCACAATAATTGTAAACCCAAAA  
TTCTGGATACAAAAGTACAATCTTTACTGTGTAAATACATGTATATGTACTATATGAAAATA  
TACCAATATCAATAATACTTATCTCTGGGTAAAAACCTCTTCTCATACCCTGTGCTAACAA  
CTTTTAACAAAAAATTTGCATCACTTTTAAGAATCAAGAAAAATTTCTGAAGGTCATATGGG  
ACAGAAAAAAAACCAAGGGAAAAATCACGCCACTTGGGAAAAAAGATTGGAATCTGCCT  
TTTTATAGATTTGTAATTAATAAGGTCCAGGCTTTCTAAGCAACTTAAATGTTTTGTTTCGA  
AACAAAGTACTTGTCTGGATGTAGGAGGAAAGGGAGTGATGTCACTGCCATTATGATGCCCC  
TTGAATATAAGACCCTACTTGCTATCTCCCCTGCACCAGCCAGGAGCCACCCATCCTCCAGC  
ACACTGAGCAGCAAGCTGGACACACGGCACACTGATCCAAATGGGTAAGGGGATGGTGGCGA  
TGCTCATTCTGGGTCTGCTACTTCTGGCGCTGCTCCTACCCGTGCAGGTTTCTTCATTTGTT  
CCTTTAACAGTATGCCGGAAGCTACTGCAGCCGAAACCACAAAGCCCTCCAACAGTGCCT  
ACAGCCTACAGCCGGTCTCCTTGTGGTCTTGCTTGCCCTTCTACATCTCTACCATTAAAGAGG  
CAGGTCAAGAAACAGCTACAGTTCTCAACCCATACACTAAAACCGAATCCAATGGTGCCT  
AGAAGTTCAATGTGGCAAGGAAAAAAACAGGTCTTCATCAAATCTACTAATTTCACTCCTT  
ATTAACAGAGAAACGCTTGAGAGTCTCAAACCTGGACTGGTTTAAAGAGCATCTGAAGGATTT  
GACTAGATGATAAATGCCTGTACTCCAGTACTTTGGGAGGCCCTAGGCCGGCGGATCACCTG  
AGGTCAGGAGTTTGAGACTAACCTGGCCAAAATGGTGAAACCCCATCTGTACTAAAAATACA  
AATATTGACTGGGCGTGGTGGTGAGTGCCTGTGATCCAGCTACTCAGGTGGCTGAAGCAGG  
ACAATCACTTGAACCTCAGGAGGCAGAGGTTGCAGTGAGCTGAGATCGCGCTACTGCACTCTA  
GCCTAGCCTGGGCAACAGAGTGAGACTTCGTCTCAAAAAAAAAAAGCCAAGTGCAGTGGCT  
CACGCCTGTAATCCCGGCACCTTTGGGAGGCCGAGGTGGGCGGATCACGAGGTCAGGAGATCA  
AGACCATCCTGGCTAATACAGTGAAACCCTGTCTCTACTAAAAATACAAAAAATTAGCCGGG  
GATGGTGGCAGGCACCTGGAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAATAGCGTGAA  
CTCAGGAGGCGGAGCTTGCAGTGAGCCGAGATTGCGCTACTGCACTCCAGCCTGGGCGACAG  
CGCGAGACTCCGTCTCAAAAAAAAAAAAAAAAAAAAAA

**FIGURE 33**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48309

><subunit 1 of 1, 67 aa, 1 stop

><MW: 6981, pI: 7.47, NX(S/T): 0

MGKGMVAMLILGLLLLALLLPVQVSSFVPLTSMPEATAAETTKPSNSALQPTAGLLVVLAL  
LHLYH

## FIGURE 34

GCCGCGGCGAGAGCGCGCCAGCCCCGCCGCGATGCCGCGCGCCAGGACGCCTCCTCCCG  
CTGCTGGCCCCGGCCGGCGCCCTGACTGCGCTGCTGCTGCTGCTGCTGGCCATGGCGGCGG  
CGGGCGCTGGGGCGCCCCGGGCCCAGGAGGCGGCGGCGGCGGCGGACGGGCCCCCGCGG  
CAGACGGCGAGGACGGACAGGACCCGACAGCAAGCACCTGTACACGGCCGACATGTTACG  
CACGGGATCCAGAGCGCCGCGCACTTCGTGCTGTTCTTCGCGCCCTGGTGTGGACACTGCCA  
GCGGCTGCAGCCGACTTGGAATGACCTGGGAGACAAATAACAGCATGGAAGATGCCAAAG  
TCTATGTGGCTAAAGTGGACTGCACGGCCCACTCCGACGTGTGCTCCGCCCAGGGGGTGCAG  
GGATACCCACCTTAAAGCTTTTCAAGCCAGGCCAAGAAGCTGTGAAGTACCAGGGTCTCG  
GGACTTCCAGACACTGGAAAAGTGGATGCTGCAGACACTGAACGAGGAGCCAGTGACACCAG  
AGCCGGAAGTGAACCGCCAGTGCCCCGAGCTCAAGCAAGGGCTGTATGAGCTCTCAGCA  
AGCAACTTTGAGCTGCACGTTGCACAAGGCGACCACTTTATCAAGTTCTTCGCTCCGTGGTG  
TGGTCACTGCAAAGCCCTGGCTCCAACCTGGGAGCAGCTGGCTCTGGGCCTTGAACATTCCG  
AACTGTCAAGATTGGCAAGGTTGATTGTACACAGCACTATGAACTCTGCTCCGGAAACCAG  
GTTCTGGCTATCCCACTCTTCTCTGGTTCCGAGATGGGAAAAGGTGGATCAGTACAAGGG  
AAAGCGGGATTGGAGTCACTGAGGGAGTACGTGGAGTGCAGCTGCAGCGCACAGAGACTG  
GAGCGAGGAGACCGTCACGCCCTCAGAGGCCCGGTGCTGGCAGCTGAGCCCGAGGCTGAC  
AAGGGCACTGTGTTGGCACTCACTGAAAATAACTTCGATGACACCATTCAGAAAGGAATAAC  
CTTCATCAAGTTTTATGCTCCATGGTGTGGTCATTGTAAGACTCTGGCTCCTACTTGGGAGG  
AACTCTCTAAAAAGGAATTCCCTGGTCTGGCGGGGGTCAAGATCGCCGAAGTAGACTGCACT  
GCTGAACGGAATATCTGCAGCAAGTATTCGGTACGAGGCTACCCACGTTATTGCTTTTCCG  
AGGAGGGAAGAAAGTCAGTGAGCACAGTGGAGGCAGAGACCTTGACTCGTTACACCGCTTG  
TCCTGAGCCAAGCGAAAGACGAACCTTAGGAACACAGTTGGAGGTCACCTCTCCTGCCCAGC  
TCCCGCACCTGCGTTTAGGAGTTCACTCCACAGAGGCCACTGGGTTCAGTGGTGGCTG  
TTCAGAAAGCAGAACATACTAAGCGTGAGGTATCTTCTTTGTGTGTGTGTTTTCCAAGCCAA  
CACACTCTACAGATTCTTTATTAAGTTAAGTTTCTCTAAGTAAATGTGTAATCATGGTCAC  
TGTGTAAACATTTTCAGTGGCGATATATCCCTTTGACCTTCTCTTGATGAAATTTACATGG  
TTTCTTTGAGACTAAAATAGCGTTGAGGGAAATGAAATTGCTGGACTATTGTGGCTCCTG  
AGTTGAGTGATTTTGGTGAAAGAAAGCACATCCAAAGCATAGTTTACCTGCCACGAGTTCT  
GGAAAGTGGCCTTGTGGCAGTATGACGTTCTCTGATCTTAAGGTCACAGTTGACTCAAT  
ACTGTGTTGGTCCGTAGCATGGAGCAGATTGAAATGCAAAAACCCACACCTCTGGAAGATA  
CTTCACGGCCGCTGCTGGAGCTTCTGTTGCTGTGAATACTTCTCTCAGTGTGAGAGTTAGC  
CGTGATGAAAGCAGCGTTACTTCTGACCGTGCTGAGTAAGAGAATGCTGATGCCATAACTT  
TATGTGTCGATACTTGTCAAATCAGTTACTGTTCAAGGGGATCCTTCTGTTTCTCACGGGGTG  
AAACATGTCTTTAGTTCTCATGTTAACACGAAGCCAGAGCCACATGAACTGTTGGATGTC  
TTCCTTAGAAAGGGTAGGCATGGAAAATTCCACGAGGCTCATTCTCAGTATCTCATTAACTC  
ATTGAAAGATTCCAGTTGTATTTGTACCTGGGGTGACAAGACCAGACAGGCTTTCCAGGC  
CTGGGTATCCAGGGAGGCTCTGCAGCCCTGCTGAAGGGCCCTAACTAGAGTTCTAGAGTTTC  
TGATTCTGTTTCTCAGTAGTCCTTTTAGAGGCTTGCTATACTTGGTCTGCTTCAAGGAGGTC  
GACCTTCTAATGTATGAAGAATGGGATGCATTTGATCTCAAGACCAAGACAGATGTCAGTG  
GGCTGCTCTGGCCCTGGTGTGCACGGCTGTGGCAGCTGTTGATGCCAGTGTCTCTAACTCA  
TGCTGTCTTGTGATTAAACACCTCTATCTCCCTTGGGAATAAGCACATAACAGGCTTAAGCT  
CTAAGATAGATAGGTGTTGTCTTTTACCATCGAGCTACTTCCCATAATAACCACTTTGCA  
TCCAACACTCTTCACCACCTCCCATACGCAAGGGGATGTGGATACTTGGCCCAAAGTAACT  
GGTGGTAGGAATCTTAGAAACAAGACCACTTATACTGTCTGTCTGAGGCAGAAGATAACAGC  
AGCATCTCGACCGCTCTGCCTTAAAGGAAATCTTTATTAATCACGTATGGTTACAGATA  
ATTCTTTTTTTTAAAAAACCCCAACCTCCTAGAGAAGCAACTGTCAAGAGTCTTGACACA  
CAACTTCAGCTTTGCATCACGAGTCTTGATTCCAAGAAAATCAAAGTGGTACAATTTGTTT  
GTTTACACTATGATACTTCTAAATAAACTCTTTTTTTTTTAA

**FIGURE 35**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA46776  
><subunit 1 of 1, 432 aa, 1 stop  
><MW: 47629, pI: 5.90, NX(S/T): 0  
MPARPGRLLPLLARPAALTALLLLLLGHGGGGRWGARAQEAADGPPAADGEDGQDPHS  
KHLTYTADMFTHTGIQSAAHFVMFFAPWCGHCQRLQPTWNDLGDKYNSMEDAKVYVAKVDCTAH  
SDVCSAQGVRGYPTLKLFPKPGQEA VKYQGP RDFQTLN WMLQTLN EEPVTPEPEVEPPSAPE  
LKQGLYEL SASNFELHVAQGDHFIKFFAPWCGHCKALAPTWEQLALGLEHSETVKIGKVDCT  
QHYELCSGNQVRGYPTLLWFRDGKKVDQYKGKRDLESLREYVESQLQRTETGATETVTPSEA  
PVLAAEPEADKGTVLALTENNFDITIAEGITFIKFYAPWCGHCKTLAPTWEELSKKEFPGLA  
GVKIAEVDCTAERNICSKYSVRGYPTLLLLFRGGKKVSEHSGGRDLDSLHRFVLSQAKDEL



**FIGURE 36**

CTTTTCTGAGGAACCAACAGCAATGAATGGCTTTGCATCCTTGCTTCGAAGAAACCAATTTAT  
CCTCCTGGTACTATTTCTTTTGCAAATTCAGAGTCTGGGTCTGGATATTGATAGCCGTCCTA  
CCGCTGAAGTCTGTGCCACACACACAATTTACCAGGACCCAAAGGAGATGATGGTGAAAAA  
GGAGATCCAGGAGAAGAGGGAAAGCATGGCAAAGTGGGACGCATGGGGCCGAAAGGAATTAA  
AGGAGAACTGGGTGATATGGGAGATCAGGGCAATATTGGCAAGACTGGGCCCCATTGGGAAGA  
AGGGTGACAAAGGGGAAAAAGGTTTGCTTGGAATACCTGGAGAAAAAGGCAAAGCAGGTACT  
GTCTGTGATTGTGGAAGATAACCGGAAATTTGTTGGACAACTGGATATTAGTATTGCTCGGCT  
CAAGACATCTATGAAGTTTGTCAAGAATGTGATAGCAGGGATTAGGGAACTGAAGAGAAAT  
TCTACTACATCGTGCAGGAAGAGAAGAACTACAGGGAATCCCTAACCCACTGCAGGATTCGG  
GGTGGAATGCTAGCCATGCCCAAGGATGAAGCTGCCAACACACTCATCGCTGACTATGTTGC  
CAAGAGTGGCTTCTTTTCGGGTGTTTCATTGGCGTGAATGACCTTGAAAGGGAGGGACAGTACA  
TGTCCACAGACAACACTCCACTGCAGAACTATAGCAACTGGAATGAGGGGGAACCCAGCGAC  
CCCTATGGTCATGAGGACTGTGTGGAGATGCTGAGCTCTGGCAGATGGAATGACACAGAGTG  
CCATCTTACCATGTACTTTGTCTGTGAGTTCATCAAGAAGAAAAAGTAACTTCCCTCATCCT  
ACGTATTTGCTATTTTCCTGTGACCGTCATTACAGTTATTGTTATCCATCCTTTTTTTCCTG  
ATTGTACTACATTTGATCTGAGTCAACATAGCTAGAAAATGCTAAACTGAGGTATGGAGCCT  
CCATCATCAAAAAAAAAAAAAAAAAA

**FIGURE 37**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50980  
><subunit 1 of 1, 277 aa, 1 stop  
><MW: 30645, pI: 7.47, NX(S/T): 2  
MNGFASLLRRNQFILLVLFLLQIQSLGLDIDS RPTAEVCATHTISPGPKGDDGEKGDGPGEEG  
KHGKVGRMGPKGIKGELGDMGDQGNIGKTGP I GKKGDKGEKGLLGIPGEK GKAGTVCD CGRY  
RK FVGQLDISIARLKTSMKFVK NVIAGIRETEEFYYIVQEEKNYRESLTHCRIRGGMLAMP  
KDEAANTLIADYVAKSGFFRVFIGVNDLEREGQYMSTDNTPLQYNSNWNEGEPSDPYGHEDC  
VEMLSSGRWNDTECHLTMYFVCEFIKKKK

**FIGURE 38**

GGTTCATATCGATTTCGAATTCGGCCACACTGGCCGGATCCTCTAGAGATCCCTCGACCTCGAC  
CCACGCGTCCGCTGCTCTCCGCCCCTGTGGAGTGGTGGGGCCCTGGGTGGGAATGGGCGTGT  
GCCAGCGCACGCGCGCTCCCTGGAAGGAGAAGTCTCAGCTAGAACGAGCGGCCCTAGGTTTT  
CGGAAGGGAGGATCAGGGATGTTTTCGAGCGGCTGGAACCAGACGGTGCCGATAGAGGAAGC  
GGGCTCCATGGCTGCCCTCCTGCTGCTGCCCTGCTGCTGTTGCTACCGCTGCTGCTGCTGA  
AGCTACACCTCTGGCCGCGAGTTGCGCTGGCTTCCGGCGGACTTGGCCTTTGCGGTGCGAGCT  
CTGTGCTGCAAAAGGGCTCTTCGAGCTCGCGCCCTGGCCGCGGCTGCCGCCGACCCGGAAGG  
TCCCGAGGGGGGCTGCAGCCTGGCCTGGCGCCTCGCGGAACCTGGCCAGCAGCGCGCCGCGC  
ACACCTTTCTCATTACGGCTCGCGGCGCTTTAGCTACTCAGAGGCGGAGCGCGAGAGTAAC  
AGGGCTGCACGCGCCTTCTACGTGCGCTAGGCTGGGACTGGGGACCCGACGGCGCGCAGAG  
CGGCGAGGGGAGCGCTGGAGAAGGCGAGCGGGCAGCGCCGGAGCCGGAGATGCAGCGGCCG  
GAAGCGGCGCGGAGTTTTCGCGGAGGGGACGGTGCCGCCAGAGGTGGAGGAGCCGCCGCCCT  
CTGTCACTGGAGCAACTGTGGCGCTGCTCCTCCCCGCTGGCCAGAGTTTCTGTGGCTCTG  
GTTCCGGCTGGCCAAGGCCGCTGCGCACTGCCTTTGTGCCACCGCCCTGCGCCGGGGCC  
CCCTGCTGCACTGCCTCCGCGCTGCGGCGCGCGCGCTGGTGCTGGCGCCAGAGTTTCTG  
GAGTCCCTGGAGCCGACCTGCCCGCTGAGAGCCATGGGGCTCCACCTGTGGGCTGCAGG  
CCCAGGAACCCACCTGTGGAATTAGCGATTTGCTGGCTGAAGTGTCCGCTGAAGTGGATG  
GGCCAGTGCCAGGATACCTCTCTCCCCCGCTGCTCGGATCAGTCATCTGAAGATCCTGCAATG  
ACCTCTGGCACACGGGCTCCCCAAGGCTGCTCGGATCAGTCATCTGAAGATCCTGCAATG  
CCAGGGCTTCTATCAGCTGTGTGGTGTCCACCAGGAAGATGTGATCTACCTCGCCCTCCAC  
TCTACCACATGTCCGTTCCCTGCTGGGCATCGTGGGCTGCATGGGCATTGGGGCCACAGTG  
GTGCTGAAATCCAAGTTCTCGGCTGGTCACTTCTGGGAAGATTGCCAGCAGCACAGGGTGAC  
GGTGTTCAGTACATTGGGGAGCTGTGCCGATACCTTGTCAACCAGCCCCGAGCAAGGCAG  
AACGTGGCCATAAGGTCCGGCTGGCAGTGGGCAGCGGGCTGCGCCAGATACCTGGGAGCGT  
TTTGTGCGGCGCTTCGGGCCCTGCAGGTGCTGGAGACATATGGACTGACAGAGGGCAACGT  
GGCCACCATCAACTACACAGGACAGCGGGCGCTGTGGGGCGTGCTTCTGGCTTTACAAGC  
ATATCTTCCCCTTCTCCTTGATTGCTATGATGTCACCACAGGAGAGCCAATTCGGGACCCC  
CAGGGGCACTGTATGGCCACATCTCCAGGTGAGCCAGGGCTGCTGGTGGCCCCGGTAAGCCA  
GCAGTCCCCATTCTGGGCTATGCTGGCGGGCCAGAGCTGGCCCGAGGGGAAGTTGCTAAAGG  
ATGTCTTCCGGCCTGGGGATGTTTTCTTCAACACTGGGGACCTGCTGGTCTGCGATGACCPA  
GGTTTTCTCCGCTTCCATGATCGTACTGGAGACACCTTCAGGTGGAAGGGGGAGAATGTGGC  
CACAACCGAGGTGGCAGAGGTCTTCGAGGCCCTAGATTTTCTTCAGGAGGTGAACGTCTATG  
GAGTCACTGTGCCAGGGCATGAAGGCAGGGCTGGAATGGCAGCCCTAGTTCTGCGTCCCCC  
CACGCTTTGGACCTTATGCAGCTCTACACCCACGTGTCTGAGAACTTGCCACCTTATGCCCC  
GCCCCGATTCCCTCAGGCTCCAGGAGTCTTTGGCCACCACAGAGACCTTCAAACAGCAGAAAG  
TTCGGATGGCAAATGAGGGCTTCGACCCACAGACCTTCTGACCCACTGTACGTTCTGGAC  
CAGGCTGTAGGTGCCTACCTGCCCCCTCAAACTGCCCGGTACAGCGCCCTCCTGGCAGGAAA  
CCTTCGAATCTGAGAACTTCCACACCTGAGGCACCTGAGAGAGGAACTCTGTGGGGTGGGG  
CCGTTGCAGGTGTACTGGGCTGTCAAGGATCTTTTCTATACCAGAACTGCGGTCACTATTTT  
GTAATAAATGTGGCTGGAGCTGATCCAGCTGTCTCTGACCTAAAAA  
AAAAAAAAAGGGCGGCCGCGACTCTAGAGTCGACCTGCAGTAGGGATAACAGGGTAATAAGC  
TTGGCCCGCATGGCCCACTTGTTTATTGCAG

**FIGURE 39**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50913  
><subunit 1 of 1, 730 aa, 1 stop  
><MW: 78644, pI: 7.65, NX(S/T): 2  
MGVCQRTAPWKEKSQLERAALGFRKGGSGMFASGWNQTVPIEEAGSMAALLLLPLLLLLLPL  
LLKLHLWPQLRWLPADLAFVRLCCKRALRARALAAAAADPEGPEGGCSLAWRLAELAQQ  
RAAHTFLIHGSRFSYSEAERESNRAARAFRLALGWDWGPDGGDSGEGSAGEGERAAPGAGD  
AAAGSGAEFAGGDGAARGGGAAAPLSPGATVALLLPAGPEFLWLWFGGLAKAGLRTAFVPTAL  
RRGPLLHCLRSCGARALVLAPEFLESLEPDLPALRAMGLHLWAAGPGTHPAGISDLLAEVSA  
EVDGPVPGYLSSPQSITDTCLYIFTSGTTGLPKAARISHLKILQCQGFYQLCGVHQEDVIYL  
ALPLYHMSGSLGIVGCMGIGATVVLKSKFSAGQFWEDCQQHRVTVFQYIGELCRYLVNQPP  
SKAERGHKVR LAVGSGLRPDTWERFVRRFGPLQVLETYGLTEGNVATINYTGQRGAVGRASW  
LYKHIFPFSLIRYDVTTGEPIRDPOGHCMATSPGEPGLLVAPVSQQSPFLGYAGGPPELAQK  
LLKDVFVRPGDVFFNTGDLVCDQGFRLRFHRTGDTFRWKGENVATTEVAEVFEALDFLQEV  
NVYGVTVPGHEGRAGMAALVLRPPHALDLMQLYTHVSENLPYARPRFLRLQESLATTETFK  
QQKVRMANEGFDPSTLSDPYVLDQAVGAYLPLTTARYSALLAGNLRI

**Signal peptide:**

aa 1-42

**CAMP- and cGMP-dependent protein kinase phosphorylation site**  
starting at aa 136

**CUB domain protein motif**

aa 254-261

**putative AMP-binding domain signature**

aa 332-343

**N-glycosylation sites**

aa 37-40 and 483-486

**FIGURE 40**

CCTGTGTTAAGCTGAGGTTTCCCCTAGATCTCGTATATCCCCAACACATACCTCCACGCACA  
CACATCCCCAAGAACCCTCGAGCTCACACCAACAGACACACGCGCGCATACACACTCGCTCTC  
GCTTGTCCATCTCCCTCCCGGGGAGCCGGCGCGCTCCCACCTTTGCCGCACACTCCGGC  
GAGCCGAGCCCGCAGCGCTCCAGGATTCTGCGGCTCGGAACCTCGGATTGCAGCTCTGAACCC  
CCATGGTGGTTTTTTAAACACTTCTTTTCTCTCTTCTCTCTGTTTGGATTGCACCGTTTCCA  
TCTGGGGGCTAGAGGAGCAAGGCAGCAGCCTTCCCAGCCAGCCCTTGTGGCTTGCCATCGT  
CCATCTGGCTTATAAAAGTTTGTCTGAGCGCAGTCCAGAGGGCTGCGCTGCTCGTCCCCCTCGG  
CTGGCAGAAGGGGGTGACGCTGGGCAGCGGCGAGGAGCGCGCCGCTGCCTCTGGCGGGCTTT  
CGGCTTGAGGGGCAAGGTGAAGAGCGCACCGGCCGTGGGGTTTACCGAGCTGGATTGTATG  
TTGCACCATGCTTCTTGGATCGGGGCTGTGATTCTTCCCCTCTTGGGGCTGCTGCTCTCCC  
TCCCCGCCGGGGCGGATGTGAAGGCTCGGAGCTGCGGAGAGGTCCGCCAGGCGTACGGTGCC  
AAGGATTGAGCCTGGCGGACATCCCCTACCAGGAGATCGCAGGGGAACACTTAAGAATCTG  
TCCTCAGGAATATACATGCTGCACCACAGAAATGGAAGACAAGTTAAGCCAACAAAGCAAAC  
TCGAATTTGAAAACCTTGTGGAAGAGACAAGCCATTTTGTGCGCACCCTTTGTGTCCAGG  
CATAAGAAATTTGACGAATTTTTCCGAGAGCTCCTGGAGAATGCAGAAAAGTCACTAAATGA  
TATGTTTGTACGGACCTATGGCATGCTGTACATGCCAGAATTGAGAAGTCTTCCAGGACCTCT  
TCACAGAGCTGAAAAGGTACTACACTGGGGGTAATGTGAATCTGGAGGAAATGCTCAATGAC  
TTTTGGGCTCGGCTCCTGGAACGGATGTTTTCAGCTGATAAACCCCTCAGTATCACTTCACTGA  
AGACTACCTGGAATGTGTGAGCAAATACACTGACCAGCTCAAGCCATTTGGAGACGTGCCCC  
GGAAACTGAAGATTGAGGTTACCCGCGCCTTCATTGCTGCCAGGACCTTTGTCCAGGGGCTG  
ACTGTGGGCAGAGAAGTTGCAAACCGAGTTTCCAAGGTGAGCCCAACCCAGGGTGTATCCG  
TGCCCTCATGAAGATGCTGTACTGCCCATACTGTGCGGGGCTTCCCACTGTGAGGCCCTGCA  
ACAACTACTGTCTCAACGTGATGAAGGGCTGCTTGGCAAATCAGGCTGACCTCGACACAGAG  
TGGAATCTGTTTATAGATGCAATGCTCTTGGTGGCAGAGCGACTGGAGGGGCCATTCAACAT  
TGAGTCGGTCATGGACCCGATAGATGTCAAGATTTCTGAAGCCATTATGAACATGCAAGAAA  
ACAGCATGCAGGTGTCTGCAAAGGTCTTTCAGGGATGTGGTCAAGCCAAACCTGCTCCAGCC  
CTCAGATCTGCCCCGCTCAGCTCCTGAAAATTTTAATACACGTTTTCAGGCCCTACAATCCTGA  
GGAAAGACCAACAACCTGCTGCAGGCACAAGCTTGGACCGGCTGGTCAAGACATAAAAGAGA  
AATTGAAGCTCTCTAAAAAGGTCTGGTCAGCATTACCCCTACACTATCTGCAAGGACGAGAGC  
GTGACAGCGGGCAGTCCAACGAGGAGGAATGCTGGAACGGGCACAGCAAAGCCAGATACTT  
GCCTGAGATCATGAATGATGGGCTCACCAACCAGATCAACAATCAGGAGGTGGATGTGGACA  
TCACTCGGCCTGACACTTTTCATCAGACAGCAGATTATGGCTCTCCGTGTGATGACCAACAAA  
CTAAAAAACGCCTACAATGGCAATGATGTCAATTTCCAGGACACAAGTGATGAATCCAGTGG  
CTCAGGGAGTGGCAGTGGGTGCATGGATGACGTGTGTCCACGGAGTTTGAGTTTGTACCA  
CAGAGGCCCCCGCAGTGGATCCCGACCGGAGAGAGGTGGACTCTTCTGCAGCCCAGCGTGGC  
CACTCCCTGCTCTCCTGGTCTCTCACCTGCATTGTCTTGGCACTGCAGAGACTGTGCAGATA  
ATCTTGGGTTTTTGGTCAGATGAAACTGCATTTTAGCTATCTGAATGGCCAACTCACTTCTT  
TTCTTACACTCTTGGACAATGGACCATGCCACAAAACTTACCGTTTTCTATGAGAAGAGAG  
CAGTAATGCAATCTGCCTCCCTTTTTGTTTTCCCAAAGAGTACCGGGTGCCAGACTGAACTG  
CTTCCTCTTCTCCTTCACTATCTGTGGGGACCTTGTATTCTAGAGAGAATTCTTACTCAA  
ATTTTTCTGTACCAGGAGATTTCTTACCTTCATTTGCTTTTATGCTGCAGAAGTAAAGGAAT  
CTCACGTTGTGAGGGTTTTTTTTTCTCATTTAAAT

**FIGURE 41**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50914  
><subunit 1 of 1, 555 aa, 1 stop  
><MW: 62736, pI: 5.36, NX(S/T): 0  
MPSWIGAVILPLLGLLLSLPAGADV KARS CGEV RQAYGAKG FSLADIPYQE IAGEHLRICPQ  
EYTCCTTEMEDKLSQQSKLEFENLVEETSHFVRTTFVSRHKKFDEFFRELLENAEKSLNDMF  
VRTYGMLYMQNSEVFQDLFTTELKRYYTGGNVNLEEMLNDFWARLLERMFQLINPOYHFSEDY  
LECVSKYTDQLKPFGDVPRKLKIQVTRAFIAARTFVQGLTVGREVANRVSKVSPTPGCIRAL  
MKMLYCPYCRGLPTVRPCNNYCLNVMKGCLANQADLDTEWNLFIDAMLLVAERLEGPFNIES  
VMDPIDVKISEAIMNMQENSMQVS AKVFQCGQPKPAPALRSARSAPENFNTFRFPYNPEER  
PTTAAGTSLDRLVTDIKEKLKLSKKVWSALPYTICKDESVTAGTSNEEECWNGH SKARYLPE  
IMNDGLTNQINNPEVDVDITRPDTFIRQQIMALRVMTNKLKNAYNGNDVNFQDTSDESSGSG  
SGSGCMDDVCPTEFEFVTTEAPAVDPDRREVDSSAAQRGHSLLSWSLTCIVLALQRLCR

**FIGURE 42A**

CGGACGCGTGGGCGGACGCGTGGGCAAAAGAACTCGGAGTGCCAAAGCTAAATAAGTTAGCT  
GAGAAAACGCACGCAGTTTGCAGCGCCTGCGCCGGGTGCGCCAACTACGCAAAGACCAAGCG  
GGCTCCGCGCGGACCGGCCGCGGGCTAGGGACCCGGCTTTGGCCTTCAGGCTCCCTAGCAG  
CGGGGAAAAGGAATTGCTGCCCGGAGTTTCTGCGGAGGTGGAGGGAGATCAGGAAACGGCTT  
CTTCTCAGTTTCGCCGCCTGGTGAGTGTGCGGGAGATTGGCAAACGCCTAGGAAAGGACTGG  
GGAAAATAGCCCTGGGAAAGTGGAGAAGGTGATCAGGAGGCCGGTCCACTACGGCAGTTTAT  
CTGTCTGATCAGAGCCAGACGCGACGCGTCCACTTCGCAGTTCTTTCCAGGTGTGGGGACCG  
CAGGACAGACGGCCGATCCCGCCGCCCTCCGTACCAGCACTCCAGGAGAGTCAGCCTCGCT  
CCCCAACGTCGAGGGCGCTCTGGCCACGAAAAGTTCTGTCCACTGTGATTCTCAATTCCTT  
GCTTGGTTTTTTTTCTCCAGAGAACTTTTGGGTGGAGATATTAACTTTTTTTTTTTTTTT  
CCTTGGTGAAGCTGCTCTAGGGAGGGGGGAGGAGGAGGAGAAAGTGAAATGTGCTGGAGAA  
GAGCGAGCCCTCCTTGTTCTTCCGGAGTCCCATCCATTAAGCCATCACTTCTGGAAGATTAA  
AGTTGTGCGACATGGTGACAGCTGAGAGGAGAGGAGGATTTCTTGCCAGGTGGAGAGTCTTC  
ACCGTCTGTTGGGTGCATGTGTGCGCCCGCAGCGGCGCGGGGCGCGTGGTTCTCCGCGTGA  
GTCTCACCTGGGACCTGAGTGAATGGCTCCAGGGGCTGTGCGGGGCATCCGCCTCCGCCTT  
CTCCACAGGCCCTGTGTCTGTCTGTGGAAGATGCTAGCAATGGGGGCGCTGGCAGGATTCTGG  
ATCCTCTGCTCCTCACTTATGGTTACCTGTCTGCGGGCCAGGCCCTAGAAGAGGAGGAAGA  
AGGGGCCTTACTAGCTCAAGCTGGAGAGAACTAGAGCCAGCACAACCTTCCACCTCCAGC  
CCCATCTCATTTTTATCCTAGCGGATGATCAGGATTTAGAGATGTGGGTACCACGGATCT  
GAGATTAAACACCTACTCTTGACAAGCTCGCTGCCGAAGGAGTTAACTGGAGAACTACTA  
TGTCCAGCCTATTTGCACACCATCCAGGAGTCAGTTTATTACTGGAAAGTATCAGATACACA  
CCGGACTTCAACATTCTATCATAAGACCTACCCAACCCAACCTGTTTACCTCTGGACAATGCC  
ACCCTACCTCAGAACTGAAGGAGGTGGATATTCAACGCATATGGTCGGAAAATGGCACTT  
GGGTTTTAAACAGAAAAGAATGCATGCCACCAGAAGAGGATTTGATACCTTTTTTGGTTCCC  
TTTTGGGAAGTGGGGATTACTATACACACTACAAATGTGACAGTCTGGGATGTGTGGCTAT  
GACTTGATGAAAACGACAATGCTGCCTGGGACTATGACAATGGCATATACTCCACACAGAT  
GTACACTCAGAGAGTACAGCAAATCTTAGCTTCCCATACCCCAAGCCTATATTTTTAT  
ATACTGCCTATCAAGCTGTTCACTACCACTGCAAGCTCCTGGCAGGTATTTGGAACACTAC  
CGATCCATTATCAACATAAAGAGGAGATGCTGCCATGCTTTCCTGCTTAGATGAAGC  
AATCAACAACGTGACATTGGCTCTAAAGACTTATGGTTTTCTATAACAACCGCATTATCATTT  
ACTCTTCAGATAATGGTGGCCAGCCTACGGCAGGAGTAACTGGCTCTCAGAGTAAAGC  
AAAGGAACATATTGGGAAGGAGGGATCCGGGCTGTAGGCTTTGTGCATAGCCCACTTCTGAA  
AAACAAGGGAACAGTGTGTAAGGAACTGTGCACATCACTGACTGGTACCCCACTCTCTTT  
CACTGGCTGAAGGACAGATTGATGAGGACATTCAACTAGATGGCTATGATATCTGGGAGACC  
ATAAGTGAGGGTCTTCGCTCACCCCGAGTAGATATTTTGCAACATTGACCCCTATACACC  
AAGGCAAAAATGGCTCCTGGGCAGCAGGCTATGGGATCTGGAACACTGCAATCCAGTCAGC  
CATCAGAGTGCAGCACTGGAAATTGCTTACAGGAAATCCTGGCTACAGCGACTGGGTCCCCC  
CTCAGTCTTTTCAGCAACCTGGGACCGAACCGGTGGCACAATGAACGGATCACCTTGTCAACT  
GGCAAAAGTGTATGGCTTTTCAACATCAGCCGACCCATATGAGAGGGTGGACCTATCTAA  
CAGGTATCCAGGAATCGTGAAGAAGCTCCTACGGAGGCTCTCACAGTTCAACAAAACCTGCAG  
TGCCGGTCAGGTATCCCCCAAAGACCCCAAGTAACCTAGGCTCAATGGAGGGGTCTGG  
GGACCATGGTATAAAGAGGAAACCAAGAAAAGAAAGCAAGCAAAAATCAGGCTGAGAAAAA  
GCAAAAGAAAAGCAAAAAAAGAAAGAAACAGCAGAAAGCAGTCTCAGGTAAACCAGCAA  
ATTTGGCTCGATAATATCGCTGGCCTAAGCGTCAGGCTTGTTCATGCTGTGCCACTCCAG  
AGACTTCTGCCACCTGGCCGCCCACTGAAAACCTGTCTGCTCAGTGCCAAGGTGCTACTCT  
TGCAAGCCCACTTAGAGAGAGTGGAGATGTTTATTTCTCTCGCTCCTTTAGAAAACGTGGT  
GAGTCTTGAGTTCAGTGTGTGCTTCACTCACTGACCAAACTGCTTTGAATTATAGGA  
GGAGAACATAACCTACCATCCGCAAGCATGCTAATTTGATGGAAGTTACAGGGTAGCATGA  
TTAAAACCTACCTTGATAAATTACAGTCAAAGATTGTGTACCTCAAAGGCCTTGAAGAATA  
TATTTTCTTGGTGAATTTTTGTATGTCTGTATGACACTTGGGTTTTTTAATTAATTTCTA  
TTTTATATATATAAATATATGTTCTTTCTGTGAAAAGCTGTTTTTCTCACATGTGAACA  
GCTTGACCTCATTTTACCATGCGTGAGGGAATGGCAATAAGAATGTTTGAGCACACTGCC  
CACAATGAATGTAACATTTTTCTAAACACTTTACTAGAAGAACATTTTCAATATAAAAAACCT  
AATTTATTTTACAGAAAAATATTTTGTGTTTTTATAAAAAGTTATGCAAAATGACTTTTAT  
TTTTATTTCTGTCATACCATTAGAAGAATTTTATTTTCAATTTCTTCAAATTATCAAGCACTGT  
AATACTATAAATTAATGTAATACTGTGTGAATTCAGACTATAAAAAACATCATTCAGAAAAAC  
TTTATAATCGTCATTGTTCAATCAAGATTTTGAATGTAATAAGATGAATATATTTCTTACAA

**FIGURE 42B**

ATTACTTGGAATTCAATGTTTGTGCAGAGTTGAGACAACTTTATTGTTTCTATCATAACT  
ATTTATGTATCTTAATTATTAAAATGATTTACTTTATGGCACTAGAAAATTTACTGTGGCTT  
TTCTGATCTAACTTCTAGCTAAAATTGTATCATTGGTCCTAAAAAATAAAAATCTTTACTAA  
TAGGCAATTGAAGGAATGGTTTGCTAACAACCACAGTAATATAATATGATTTTACAGATAGA  
TGCTTCCCCTTGGCTATGACATGGAGAAAAGATTTTCCCATATAATAACTAATATTTATATT  
AGGTTGGTGCAAACTAGTTGCGGTTTTTCCCATTAAGTAATAACCTTACTCTTATACAA  
AGTGGACACTGTGGGGAGATACAGAGAAATGGAAGATACGGATCCTGCCTGGAGTAGGTAAC  
CTTGCTTGGAACCCCATGCAAACGTCATGAGGAGAATTAAAGGAGTATTATCAGTAATG  
AAGTTTATCATGGGTCATCAATGAGCATAGATTGGTGTGGATCCTGTAGACCCTGGTGT  
CTTTGAAGTGCCCTCTCCTAATGCAGAGGCCTTGAAGCTTACAGTATACACTTGAAAAGTCA  
CAGATAGCTAGAATTATGATCTTTGAAGTTATAACTGTGATCTGAAAATGTGTGTGGTGGTA  
TGACAGCATACCATTAAATACATTTACATCACAGCTCAAAGGACTGTGATATAATCCATTTA  
TATCAAACTCAAAGGACTGTGATATAATCCATTTATATCACAGCTCACAGTTTCTGAAAAT  
GTATAAAAGAATCTATAATCTAGTACTGAAATTACTAAATTGGGTAAGATGATTTAAATGAT  
TTTAATTTTAACATTTTATTTCTAGAATATATGGCTCCATTTTATTTTATAGTGTAAGTTG  
TATTTCCTAAGTTTGTGTTTTGTGCGACAGTATCTTTTAAATGAGTCTTAAAAATAAAGGCA  
TATTGTTTATGTTTAAA  
AAA



**FIGURE 43**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48296  
><subunit 1 of 1, 515 aa, 1 stop  
><MW: 56885, pI: 6.49, NX(S/T): 5  
MAPRGCAGHPPPPSPQACVCPGKMLAMGALAGFWILCLLTYGYLSWGQALEEEEEGALLAQA  
GEKLEPSTTSTSQPHLIFILADDQGFRDVGYPHGSEIKTPTLDKLAAEGVKLENYVQPICTP  
SRSQFITGKYQIHTGLQHSIIRPTQPNCLPLDNATLPQKLKEVGYSTHMGKWHLGFNKEC  
MPTRRGFDFTFFGSLGSGDYTHYKCDSPGMCYDLYENDNAAWDYDNGIYSTQMYTQRVQQ  
ILASHNPTKPIFLYTAYQAVHSPQLQAPGRYFEHYRSIININRRRYAAMLSCLDEAINNVTLA  
LKTYGFYNNNSIIYSSDNGGQPTAGGSNWPLRGSKGTYWEGGIRAVGFVHSPLLKNKGTVCK  
ELVHITDWPYPTLISLAEGQIDEDIQLDGYDIWETISEGLRSPRVDILHNIDPYTPRQKMAPG  
QQAMGSGTLQSSQSECSTGNCLQEILATATGSPLSLSATWDRTGGTMNGSPCQLAKVYGFS  
TSQPTHMRGWYTLTGIOES

**Important Features:****Signal Peptide:**

amino acids 1-37

**Sulfatases signature 1.**

amino acids 120-132

**Sulfatases signature 2.**

amino acids 168-177

**Tyrosine kinase phosphorylation site.**

amino acids 163-169

**N-glycosylation sites.**

amino acids 157-160, 306-309 and 318-321

**FIGURE 44**

CGGACGCGTGGGTGCGAGTGGAGCGGAGGACCCGAGCGGCTGAGGAGAGAGGAGGCGGCGGC  
TTAGCTGCTACGGGGTCCGGCCGGCGCCCTCCCGAGGGGGGCTCAGGAGGAGGAAGGAGGAC  
CCGTGCGAGAATGCCTCTGCCCTGGAGCCTTGCCTCCCGCTGCTGCTCTCTGGGTGGCAG  
GTGGTTTCGGGAACGCGGCCAGTGCAGGCATCACGGGTTGTTAGCATCGGCACGTACGCT  
GGGTCTGTCACTATGGAATAAAGTGGCCTGCTGCTACGGCTGGAGAAGAAACAGCAAGGG  
AGTCTGTGAAGCTACATGCGAACCTGGATGTAAGTTGGTGAGTGCCTGGGACCAACAAAT  
GCAGATGCTTTCCAGGATACACCGGGAAAACCTGCAGTCAAGATGTGAATGAGTGTGGAATG  
AAACCCGGCCATGCCAACACAGATGTGTGAATACACACGGAAGCTACAAGTGCTTTTGCT  
CAGTGGCCACATGCTCATGCCAGATGCTACGTGTGTGAAGTCTAGGACATGTGCCATGATAA  
ACTGTGAGTACAGCTGTGAAGACACAGAAGAAGGGCCACAGTGCCTGTGTCCATCCTCAGGA  
CTCCGCTGGCCCCAAATGGAAGAGACTGTCTAGATATTGATGAATGTGCCTCTGGTAAAGT  
CATCTGTCCCTACAATCGAAGATGTGTGAACACATTTGGAAGCTACTACTGCAAATGTCACA  
TTGGTTTCGAAATGCAATATATCAGTGGACGATATGACTGTATAGATATAAATGAATGTACT  
ATGGATAGCCATACGTGCAGCCACCATGCCAATTGCTTCAATACCCAAGGGTCTTCAAGTG  
TAAATGCAAGCAGGGATATAAAGGCAATGGACTTCGGTGTTCTGCTATCCCTGAAAATTTCTG  
TGAAGGAAGTCTCAGAGCACCTGGTACCATCAAAGACAGAATCAAGAAGTTGCTTGCTCAC  
AAAAACAGCATGAAAAAGAAGGCAAAAATTAATAATGTTACCCCAAGAACCCACAGGACTCC  
TACCCCTAAGGTGAAGTTCAGGCCCTTCAACTATGAAGAGATAGTTTCCAGAGGCGGGAAGT  
CTCATGGAGGTAAAAAAGGGAATGAAGAGAAATGAAGAGGGGCTTGAGGATGAGAAAAGAG  
AAGAGAAAGCCCTGAAGAATGACATAGAGGAGCGAAGCCTGCGAGGAGATGTGTTTTTCCCT  
AAGGTGAATGAAGCAGGTGAATTCGGCCTGATTCTGGTCCAAAGGAAAGCGCTAACTTCCAA  
ACTGGAACATAAAGATTTAAATATCTCGGTTGACTGCAGCTTCAATCATGGGATCTGTGACT  
GGAACAGGATAGAGAAGATGATTTTACTGGAATCCTGCTGATCGAGATAATGCTATTGGC  
TTCTATATGGCAGTTCCGGCCTTGGCAGGTCAAGAAAGACATTGGCCGATTGAAACTTCT  
CCTACCTGACCTGCAACCCCAAAGCAACTTCTGTTTGCTCTTTGATTACCGGCTGGCCGGAG  
ACAAAGTCCGGGAACTTTCAGTGTGTTGTGAAAAACAGTAACAATGCCCTGGCATGGGAGAAG  
ACCACGAGTGAGGATGAAAAGTGAAGACAGGGAAAATTGAGTTGTATCAAGGAACTGATGC  
TACCAAAGCATCATTTTTGAAGCAGAACGTGGCAAGGGCAAAACCGGCGAAATCGCAGTGG  
ATGGCCTCTTGCTTGTTCAGGCTTATGTCCAGATAGCCTTTTCTGTGGATGACTGAATG  
TTACTATCTTTATATTTGACTTTGTATGTGAGTCCCTGGTTTTTTTGATATTGCATCATAG  
GACCTCTGGCATTTTAGAACTTAGCTGAAAAATTGTAATGTACCAACAGAAATATTATTG  
TAAGATGCCTTTCTTGATATAAGATATGCCAATATTGCTTTAAATATCATATCACTGTATCT  
TCTCAGTCATTTCTGAATCTTTCCNCATTATATTATAAATNTGGAAANGTCAGTTTATCTC  
CCCTCCTCNGTATATCTGATTTGTATANGTANGTTGATGNGCTTCTCTCTACAACATTTCTA  
GAAATAGAAAAAAAAGCACAGAGAAATGTTAACTGTTTGACTCTTATGATACTTCTTGGA  
AACTATGACATCAAAGATAGACTTTTGCTAAGTGGCTTAGCTGGGTCTTTCATAGCCAAAC  
TTGTATATTTAATCTTTGTAATAATAA

**FIGURE 45**

MPLPWSLALPLLLSWVAGGFGNAASARHHGLLASARQPGVCHYGTKLACCYGWRNSKGVCE  
ATCEPGCKFGECVGPNNKCRFCFPGYTGKTCSQDVNECGMKPRPCQHRVCNTHGSYKCFCLSGH  
MLMPDATCVNSRTCAMINCQYSCEDTEEGPQCLCPSSGLRLAPNGRDCLDIDECASGKVICP  
YNNRCVNTFGSYYCKCHIGFELQYISGRYDCIDINECTMDSHTCSHHANCFNTQGSFKCKCK  
QGYKGNGLRCSAIPENSVKEVLRAPGTIKDRIKKLLAHKNSMKKKAKIKNVTPEPTRTPPK  
VNLQPFNYEEIVSRGGNSHGGKKGNEEK

**Signal peptide:**

amino acids 1-21

**EGF-like domain cysteine pattern signature.**

amino acids 80-91

**Calcium-binding EGF-like domains**

amino acids 103-124, 230-251 and 185-206

**FIGURE 46**

GGGAGCTGCTGCTGTGGCTGCTGGTGCTGTGCGCGCTGCTCCTGCTCTTGGTGCAGCTGCTG  
CGCTTCCTGAGGGCTGACGGCGACCTGACGCTACTATGGGCCGAGTGGCAGGGACGACGCCC  
AGAATGGGAGCTGACTGATATGGTGGTGTGGGTGACTGGAGCCTCGAGTGGGAATTGGTGAGG  
AGCTGGCTTACCAGTTGTCTAAACTAGGAGTTTCTCTTGCTGTGCTCAGCCAGAAGAGTGCAT  
GAGCTGGAAAGGGTGAAAAGAAGATGCCTAGAGAATGGCAATTTAAAAGAAAAAGATATACT  
TGTTTTGCCCCCTTGACCTGACCGACACTGGTTCCCATGAAGCGGCTACCAAAGCTGTTCTCC  
AGGAGTTTGGTAGAATCGACATTCTGGTCAACAATGGTGGAATGTCCCAGCGTTCTCTGTGC  
ATGGATACCAGCTTGATGTCTACAGAAAGCTAATAGAGCTTAACTACTTAGGGACGGTGTC  
CTTGACAAAATGTGTTCTGCCTCACATGATCGAGAGGAAGCAAGGAAAGATTGTTACTGTGA  
ATAGCATCCTGGGTATCATATCTGTACCTCTTTCCATTGGATACTGTGCTAGCAAGCATGCT  
CTCCGGGGTTTTTTTTAATGGCCTTCGAACAGAACTTGCCACATACCCAGGTATAATAGTTTC  
TAACATTTGCCCAGGACCTGTGCAATCAAATATTGTGGAGAATTCCCTAGCTGGAGAAGTCA  
CAAAGACTATAGGCAATAATGGAGACCAGTCCCAAGATGACAACCAGTCGTTGTGTGCGG  
CTGATGTTAATCAGCATGGCCAATGATTTGAAAGAAGTTTGGATCTCAGAACAACCTTTCTT  
GTTAGTAACATATTTGTGGCAATACATGCCAACCTGGGCCTGGTGGATAACCAACAAGATGG  
GGAAGAAAAGGATTGAGAACTTTAAGAGTGGTGTGGATGCAGACTCTTCTTATTTTAAAATC  
TTTAAGACAAAACATGACTGAAAAGAGCACCTGTACTTTTCAAGCCACTGGAGGGAGAAATG  
GAAAACATGAAAACAGCAATCTTCTTATGCTTCTGAATAATCAAAGACTAATTTGTGATTTT  
ACTTTTTAATAGATATGACTTTGCTTCCAACATGGAATGAAATAAAAAATAAATAATAAAG  
ATTGCCATGAATCTTGCAAAA

**FIGURE 47**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA36343

><subunit 1 of 1, 289 aa, 1 stop

><MW: 32268, pI: 9.21, NX(S/T): 0

MVVWVTGASSGIGEELAYQLSKLGVSLVLSARRVHELERVKRRCLEENGLKEKDILVLPDL  
TDTGSHEAATKAVLQEFGRIDILVNNGGMSQRSCLMDTSLDVYRKLIELNYLGTVSLTKCVL  
PHMIERKQGKIVTVNSILGIISVPLSIGYCASKHALRGFFNGLRTELATYPGIIVSNICPGP  
VQSNIVENSLAGEVTKTIGNNGDQSHKMTTSRCVRLMLISMANDLKEVWISEQPFLLVTYLW  
QYMPWAWWITNKMGGKRIENFKSGVDADSSYFKIFKTKHD

**Important Features:****Signal Peptide:**

amino acids 1-31

**Transmembrane domain:**

amino acids 136-157

**Tyrosine kinase phosphorylation site.**

106-113 and 107-114

**Homologous region to Short-chain alcohol dehydrogenase**  
amino acids 80-90, 131-168, 1-13 and 176-185

**FIGURE 48**

CGACGTGGGCACCGCCATCAGCTGTTTCGCGCGTCTTCTCCTCCAGGTGGGGCAGGGGTTTC  
GGGCTGGTGGAGCATGTGCTGGGACAGGACAGCATCCTCAATCAATCCAACAGCATATTTCGG  
TTGCATCTTCTACACACTACAGCTATTGTTAGGTTGCCTGCGGACACGCTGGGCCCTGTGTCC  
TGATGCTGCTGAGCTCCCTGGTGTCTCTCGCTGGTTCTGTCTACCTGGCCTGGATCCTGTTT  
TTCGTGCTCTATGATTTCTGCATTGTTTGTATCACCACCTATGCTATCAACGTGAGCCTGAT  
GTGGCTCAGTTTCCGGAAGGTCCAAGAACCCAGGGCAAGGCTAAGAGGCACTGAGCCCTCA  
ACCCAAGCCAGGCTGACCTCATCTGCTTTGCTTTGGTCTTCAAGCCGCTCAGCGTGCCTGTG  
GACAGCGTGGCCCCGGCCCCCAAGCCTCAGGAGGGCAACACAGTCCCTGGCGAGTGGCCCC  
TGGCAGGCCAGTGTGAGGAGGCAAGGAGCCACATCTGCAGCGGCTCCCTGGTGGCAGACAC  
CTGGGTCTTCACTGCTGCCCAGTCTTTGAAAAGGCAGCAGCAACAGAACTGAATTCCTGGT  
CAGTGGTCTTGGGTTCTCTGCAGCGTGAAGGACTCAGCCCTGGGGCCGAAGAGGTGGGGGTG  
GCTGCCCTGCAGTTGCCAGGGCCTATAACCACTACAGCCAGGGCTCAGACCTGGCCCTGCT  
GCAGCTCGCCACCCACGACCCACACACCCCTCTGCCTGCCCCAGCCGCCCCATCGCTTCC  
CCTTTGGAGCCTCCTGCTGGGCCACTGGCTGGGATCAGGACACCACTGATGCTCCTGGGACC  
CTACGCAATCTGCGCTGCGTCTCATCAGTCGCCCCACATGTAACGTATCTACAACCACT  
GCACCAGCGACACCTGTCCAACCCGGCCCCGGCCTGGGATGCTATGTGGGGGCCCCCAGCCTG  
GGGTGCAGGGCCCCCTGTCAGGGAGATTCCGGGGGCCCTGTGCTGTGCCTCGAGCCTGACGGA  
CACTGGGTTTCAAGCTGGCATCATCAGCTTTGCATCAAGCTGTGCCAGGAGGACGCTCCTGT  
GCTGCTGACCAACACAGCTGCTCACAGTTTCTGGCTGCAGGCTCGAGTTCAAGGGGGCAGCTT  
TCCTGGCCCAGAGCCCAGAGACCCCGGAGATGAGTGATGAGGACAGCTGTGTAGCCTGTGGA  
TCCTTGAGGACAGCAGGTCCCCAGGCAGGAGACCCCTCCCCATGGCCCTGGGAGGCCAGGCT  
GATGCACCAGGACAGCTGGCCTGTGGCGGAGCCCTGGTGTGAGAGGAGGCGGTGCTAACTG  
CTGCCCAGTCTTTCATTGGGCGCCAGGCCCCAGAGGAATGGAGCGTAGGGCTGGGGACAGAG  
CCGGAGGAGTGGGGCCTGAAGCAGCTCATCCTGCATGGAGCCTACACCCACCCTGAGGGGGG  
CTACGACATGGCCCTCCTGCTGCTGGCCCAGCCTGTGACACTGGGAGCCAGCCTGCGGCCCC  
TCTGCTGCCCCTATCCTGACCACCACCTGCCTGATGGGGAGCGTGGCTGGGTTCTGGGACGG  
GCCCCCCCAGGAGCAGGCATCAGCTCCCTCCAGACAGTGGCCGTGACCCTCCTGGGGCCTAG  
GGCCTGCAGCCGGCTGCATGCAGCTCCTGGGGGTGATGGCAGCCCTATTCTGCCGGGGATGG  
TGTGTACCAATGCTGTGGGTGAGCTGCCCAGCTGTGAGGGCCCTGTCTGGGGCACCACTGGTG  
CATGAGGTGAGGGGCACATGGTTCTTGGCCGGGCTGCACAGCTTCGGAGATGCTTGCCAAGG  
CCCCGCCAGGCCGGCGGTCTTCACCGCGCTCCCTGCCTATGAGGACTGGGTGAGCAGTTTGG  
ACTGGCAGGTCTACTTCGCCGAGGAACCAAGAGCCGAGGCTGAGCCTGGAAGCTGCCTGGCC  
AACATAAGCCAACCAACCAAGCTGCTGACAGGGGACCTGGCCATTCTCAGGACAAGAGAATGC  
AGGCAGGCAATGGCATTACTGCCCCCTGTCTCCCCACCCTGTCTGTGTGATTCCAGGCAC  
CAGGGCAGGGCCAGAGCCAGCAGCTGTGGGAAGGAACCTGCCTGGGGCCACAGGTGCCCA  
CTCCCCACCCTGCAGGACAGGGGTGTCTGTGGACACTCCCACACCCAACTCTGCTACCAAGC  
AGGCGTCTCAGCTTTCCTCCTCTTACTCTTTCAGATACAATCACGCCAGCCACGTTGTTT  
TGAAAATTTCTTTTTTTGGGGGGCAGCAGTTTCTTTTTTAACTTAAATAAATGTTTAC  
AAAATAAAA

**FIGURE 49**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA40571  
MLLSSLVSLAGSVYLAWILFFVLYDFCIVCITTYAINVSLMWLSFRKVQEPQGKAKRHGNTV  
PGEWPWQASVRRQGAHICSGSLVADTWVLTAAHCFEKAAATELNSWSVVLGSLQREGLSPGA  
EEVGVAALQLPRAYNHYSQGSDDLALLQLAHPTTHTPLCLPQPAHRFPFGASCWATGWDQDTS  
DAPGTLRNLRLRLISRPTCNCIYNQLHQHLSNPARPGMLCGGPQPGVQGPCQGDSSGGPVLC  
LEPDGHWVQAGIISFASSCAQEDAPVLLTNTAAHSSWLQARVQGAAFLAQSPETPEMSDEDS  
CVACGSLRTAGPQAGAPSPWPWEARLMHQQLACGGALVSEEAVLTAHCFIGRQAPEEWSV  
GLGTRPEEWGLKQLILHGAYTHPEGGYDMALLLLAQPVTLGASLRPLCLPYPDHHLPDGERG  
WVLGRARPGAGISSLOTVPVTLGPRACSRLLHAAPGGDGSPILPGMVCTSAVGELPSCEGLS  
GAPLVHEVRGTWFLAGLHSFGDACQGPAPPAVFTALPAYEDWVSSLDWQVYFAEEPEPEAEPE  
GSCLANISQPTSC

**Important features:**

**Signal peptide:**

amino acids 1-15

**Homologous region to Serine proteases, trypsin family**  
amino acids 79-95, 343-359 and 237-247

**N-glycosylation sites.**

amino acids 37-40 and 564-567

**Kringle domains**

amino acids 79-96, 343-360 and 235-247

**FIGURE 50**

CGGGCCGCCCCCGGCCCCCATTCGGGCGGGCCCTCGCTGCGGCGGCGACTGAGCCAGGCTGG  
GCCGCGTCCCTGAGTCCCAGAGTCGGCGCGGCGCGGCAGGGGCAGCCTTCCACCACGGGGAG  
CCCAGCTGTCAGCCGCCTCACAGGAAGATGCTGCGTCGGCGGGGCAGCCCTGGCATGGGTGT  
GCATGTGGGTGCAGCCCTGGGAGCACTGTGGTTCTGCCTCACAGGAGCCCTGGAGGTCCAGG  
TCCCTGAAGACCCAGTGGTGGCACTGGTGGGCACCGATGCCACCCTGTGCTGCTCCTTCTCC  
CCTGAGCCTGGCTTCAGCCTGGCACAGCTCAACCTCATCTGGCAGCTGACAGATACCAAACA  
GCTGGTGCACAGCTTTGCTGAGGGCCAGGACCAGGGCAGCGCTATGCCAACCGCACGGCCC  
TCTTCCCGGACCTGCTGGCACAGGGCAACGCATCCCTGAGGCTGCAGCGCGTGCCTGTGGCG  
GACGAGGGCAGCTTCACCTGCTTCGTGAGCATCCGGGATTTCCGCAGCGCTGCCGTGAGCCT  
GCAGGTGGCCGCTCCCTACTCGAAGCCCAGCATGACCCTGGAGCCCAACAAGGACCTGCGGC  
CAGGGGACACGGTGACCATCACGTGCTCCAGCTACCAGGGCTACCCTGAGGCTGAGGTGTTT  
TGGCAGGATGGGCAGGGTGTGCCCCTGACTGGCAACGTGACCACGTGCGAGATGGCCAACGA  
GCAGGGCTTGTTTGATGTGCACAGCGTCTGCGGGTGGTGTGGGTGCGAATGGCACCTACA  
GCTGCCTGGTGCGCAACCCCGTGTGTCAGCAGGATGCGCACRGCTCTGTCAACATCACAGGG  
CAGCCTATGACATTTCCCCCAGAGGCCCTGTGGGTGACCGTGGGGCTGTCTGTCTGTCTCAT  
TGCACTGCTGGTGGCCCTGGCTTTTCGTGTGCTGGAGAAAGATCAAACAGAGCTGTGAGGAGG  
AGAATGCAGGAGCTGAGGACCAGGATGGGGAGGGAGAAGGCTCCAAGACAGCCCTGCAGCCT  
CTGAAACACTCTGACAGCAAAGAAGATGATGGACAAGAAATAGCCTGACCATGAGGACCAGG  
GAGCTGCTACCCCTCCCTACAGCTCCTACCCCTCTGGCTGCAATGGGGCTGCACTGTGAGCCC  
TGCCCCCAACAGATGCATCCTGCTCTGACAGGTGGGCTCCTTCTCCAAAGGATGCGATACAC  
AGACCACTGTGCAGCCTTATTTCTCCAATGGACATGATTCCCAAGTCATCCTGCTGCCCTTT  
TTCTTATAGACACAATGAACAGACCACCCACAACCTTAGTTCTCTAAGTCATCCTGCCTGCT  
GCCTTATTTACAGTACATACATTTCTTAGGGACACAGTACACTGACCACATCACCACCCTC  
TTCTTCCAGTGCTGCGTGGACCATCTGGCTGCCCTTTTTTCTCCAAAGATGCAATATTCAGA  
CTGACTGACCCCTGCCTTATTTACCAAAGACACGATGCATAGTCACCCCGGCCTTGTTTC  
TCCAATGGCCGTGATACACTAGTGATCATGTTTCAGCCCTGCTTCCACCTGCATAGAATCTTT  
TCTTCTCAGACAGGGACAGTGCGGCCTCAACATCTCCTGGAGTCTAGAAGCTGTTTCTTTTC  
CCCTCCTTCTCCTGCCCCAAGTGAAGACAGGGCAGGGCCAGGAATGCTTTGGGGACACCG  
AGGGGACTGCCCCCACCACCATGGTGCTATTCTGGGGCTGGGGCAGTCTTTTCTGGC  
TTGCCTCTGGCCAGCTCCTGGCCTCTGGTAGAGTGAGACTTCAGACGTTCTGATGCCTTCCG  
GATGTCATCTCTCCCTGCCCCAGGAATGGAAGATGTGAGGACTTCTAATTTAAATGTGGGAC  
TCGGAGGGATTTTGTAACCTGGGGTATATTTTGGGGAAAATAAATGTCTTTGTAAAAAAA  
AAAAAAAAAAAAA



**FIGURE 51**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA41386  
><subunit 1 of 1, 316 aa, 1 stop, 1 unknown  
><MW: -1, pI: 4.62, NX(S/T): 4  
MLRRRGSPGMGVHVGAAALGALWFCLTGALEVQVPEDPVVALVGTDATLCCSFSPPEPGFSLAQ  
LNLIWQLTDTKQLVHSFAEGQDQGSAYANRTALFPDLLAQGNASRLRLQVRVVADEGSFTCFV  
SIRDFGSAAVSLQVAAPYSKPSMTLEPNKDLRPGDTVTITCSSYQGYPEAEVFWQDGQGVPL  
TGNVTTSQMANEQGLFDVHSVLRVVLGANGTYSLVRNPVLQQDAHXSVTITGQPMTFPPEA  
LWVTVGLSVCLIALLLVALAFVCWRRIKIQSCEEENAGAEDQDGEGECSKTALQPLKHSDSKED  
DGQEIA

**Important features:****Signal peptide:**

amino acids 1-28

**Transmembrane domain:**

amino acids 251-270

**N-glycosylation site.**

amino acids 91-94, 104-107, 189-192 and 215-218

**Homologous region to Immunoglobulins and MHC**

amino acids 217-234

**FIGURE 52**

TTCGTGACCCTTGAGAAAAGAGTTGGTGGTAAATGTGCCACGTCTTCTAAGAAGGGGGAGTC  
CTGAACTTGTCTGAAGCCCTTGTCCGTAAGCCTTGAACCTACGTTCTTAAATCTATGAAGTCG  
AGGGACCTTTCGCTGCTTTTGTAGGGACTTCTTTCCTTGCTTCAGCAACATGAGGCTTTTCT  
TGTGGAACGCGGTCTTGACTCTGTTTCGTCACTTCTTTGATTGGGGCTTTGATCCCTGAACCA  
GAAGTGAAAATTGAAGTTCTCCAGAAGCCATTCTGTCATCGCAAGACCAAAGGAGGGGA  
TTTGATGTTGGTCCACTATGAAGGCTACTTAGAAAAGGACGGCTCCTTATTTCACTCCACTC  
ACAAACATAACAATGGTCAGCCCATTGTTTACCCTGGGCATCCTGGAGGCTCTCAAAGGT  
TGGGACCAGGGCTTGAAAGGAATGTGTGTAGGAGAGAAGAGAAAGCTCATCATTCCTCCTGC  
TCTGGGCTATGGAAAAGAAGGAAAAGGTAAATTTCCCCAGAAAGTACACTGATATTTAATA  
TTGATCTCCTGGAGATTCGAAATGGACCAAGATCCCATGAATCATTTCCAAGAAATGGATCTT  
AATGATGACTGGAACTCTCTAAAGATGAGGTTAAAGCATATTTAAAGAAGGAGTTTGAAAA  
ACATGGTGCGGTGGTGAATGAAAGTCATCATGATGCTTTGGTGGAGGATATTTTTTGATAAAG  
AAGATGAAGACAAAGATGGGTTTATATCTGCCAGAGAATTTACATATAAACACGATGAGTTA  
TAGAGATACATCTACCCTTTTAATATAGCACTCATCTTTCAAGAGAGGGCAGTCATCTTTAA  
AGAACATTTTATTTTTTATACAATGTTCTTTCTTGCTTTGTTTTTTATTTTTTATATATTTTTT  
CTGACTCCTATTTAAAGAACCCCTTAGGTTTCTAAGTACCCATTCTTTCTGATAAGTTATT  
GGGAAGAAAAAGCTAATTGGTCTTTGAATAGAAGACTTCTGGACAATTTTTTCACTTTCACAG  
ATATGAAGCTTTGTTTTACTTTCTCACTTATAAATTTAAATGTTGCAACTGGGAATATAACC  
ACGACATGAGACCAGGTTATAGCACAAATTAGCACCCCTATATTTCTGCTTCCCTCTATTTTC  
TCCAAGTTAGAGGTCAACATTTGAAAAGCCTTTTGCAATAGCCCAAGGCTTGCTATTTTCAT  
GTTATAATGAAATAGTTTATGTGTAACCTGGCTCTGAGTCTCTGCTGAGGACCCAGAGGAAAA  
TGGTTGTTGGACCTGACTTGTTAATGGCTACTGCTTTACTAAGGAGATGTGCAATGCTGAAG  
TTAGAAACAAGGTTAATAGCCAGGCATGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGAG  
GCTGAGGCGGGCGGATCACCTGAGGTTGGGAGTTGAGACACAGCCTGACCAACACGGAGAAA  
CCCTATCTCTACTAAAAATACAAAGTAGCCCGGCGTGGTGATGCGTGCTGTAATCCCAGCT  
ACCCAGGAAGGCTGAGGCGGCAGAATCACTTGAACCCGAGGCCGAGGTTGCGGTAAGCCGAG  
ATCACCTNCAGCCTGGACACTCTGTCTCGAAAAAAGAAAAGAACACGGTTAATACCATATNA  
ATATGTATGCATTGAGACATGCTACCTAGGACTTAAGCTGATGAAGCTTGGCTCCTAGTGAT  
TGGTGGCCTATTATGATAAATAGGACAAATCATTTATGTGTGAGTTTCTTTGTAATAAAATG  
TATCAATATGTTATAGATGAGGTAGAAAGTTATATTTATATTCAATATTTACTTCTTAAGGC  
TAGCGGAATATCCTTCCTGGTTCTTTAATGGGTAGTCTATAGTATATTATACTACAATAACA  
TTGTATCATAAGATAAAGTAGTAAACCAGTCTACATTTTCCCATTTCTGTCTCATCAAAAAC  
TGAAGTTAGCTGGGTGTGGTGGCTCATGCCTGTAATCCCAGCACTTTGGGGGCCAAGGAGGG  
TGGATCACTTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTCTA  
CTAAAAATACAAAAATTAGCCAGGCGTGGTGGTGACACCTGTAGTCCCAGCTACTCGGGAG  
GCTGAGACAGGAGATTTGCTTGAACCCGGGAGGCGGAGGTTGCAGTGAGCCAAGATTGTGCC  
ACTGCACTCCAGCCTGGGTGACAGAGCAAGACTCCATCTCAAAAAAAAAAAAAAGAAGCAGA  
CCTACAGCAGCTACTATTGAATAAATACCTATCCTGGATTTT

**FIGURE 53**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44194  
><subunit 1 of 1, 211 aa, 1 stop  
><MW: 24172, pI: 5.99, NX(S/T): 1  
MRLFLWNAVLTFLVFTSLIGALIPPEVKIEVLQKPFICHRKTKGGDLMLVHYEGYLEKDGSL  
FHSTHKHNNNGQPIWFITLGILEALKGWDQGLKGMCVGEKRKLIIPPALGYGKEGKGKIPPEST  
LIFNIDLLEIRNGPRSHESFQEMDLNDDWKLSKDEVKAYLKKEFEKHGAVVNESHHDALVED  
IFDKEDDKDGFISAREFTYKHDEL

**Important features:**

**Signal peptide:**

amino acids 1-20

**N-glycosylation site.**

amino acids 176-179

**Casein kinase II phosphorylation site.**

amino acids 143-146, 156-159, 178-181 and 200-203

**Endoplasmic reticulum targeting sequence.**

amino acids 208-211

**FKBP-type peptidyl-prolyl cis-trans isomerase**

amino acids 78-114 and 118-131

**EF-hand calcium-binding domain.**

amino acids 191-203, 184-203 and 140-159

**S-100/ICaBP type calcium binding domain**

amino acids 183-203

**FIGURE 54**

AATAAAGCTTCCTTAATGTTGTATATGTCTTTGAAGTACATCCGTGCATTTTTTTTTTAGCAT  
CCAACCATTCCTCCCTTGTAGTTCTCGCCCCCTCAAATCACCTCTCCCGTAGCCCACCCGA  
CTAACATCTCAGTCTCTGAAAATGCACAGAGATGCCTGGCTACCTCGCCCTGCCTTCAGCCT  
CACGGGGCTCAGTCTCTTTTTCTCTTTGGTGCCACCAGGACGGAGCATGGAGGTCACAGTAC  
CTGCCACCCTCAACGTCTCAATGGCTCTGACGCCCCGCTGCCCTGCACCTTCAACTCCTGC  
TACACAGTGAACCACAAACAGTTCTCCCTGAACTGGACTTACCAGGAGTGCAACAACCTGCTC  
TGAGGAGATGTTCCCTCCAGTTCCGCATGAAGATCATTAACCTGAAGCTGGAGCGGTTTCAAG  
ACCGCGTGGAGTTCTCAGGGAACCCAGCAAGTACGATGTGTGGTGATGCTGAGAAACGTG  
CAGCCGGAGGATGAGGGGATTTACAACTGCTACATCATGAACCCCCCTGACCGCCACCGTGG  
CCATGGCAAGATCCATCTGCAGGTCTCATGGAAGAGCCCCCTGAGCGGGACTCCACGGTGG  
CCGTGATTGTGGGTGCCTCCGTGGGGGCTTCTGGCTGTGGTCATCTTGGTGCTGATGGTG  
GTCAAGTGTGTGAGGAGAAAAAAGAGCAGAAGCTGAGCACAGATGACCTGAAGACCGAGGA  
GGAGGGCAAGACGGACGGTGAAGGCAACCCGGATGATGGCGCCAAGTAGTGGGTGGCCGGCC  
CTGCAGCCTCCCGTGTCCCGTCTCCTCCCCCTCTCCGCCCTGTACAGTGACCCTGCCTGCTCG  
CTCTTGGTGTGCTTCCCGTGACCTAGGACCCAGGGCCACCTGGGGCCTCCTGAACCCCCG  
ACTTCGTATCTCCACCCCTGCACCAAGAGTGACCCACTCTCTTCCATCCGAGAAACCTGCCA  
TGCTCTGGGACGTGTGGGCCCTGGGGAGAGGAGAGAAAGGGCTCCACCTGCCAGTCCCTGG  
GGGAGGCAGGAGGCACATGTGAGGGTCCCCAGAGAGAAGGGAGTGGGTGGGCAGGGGTAGA  
GGAGGGGCCGTGTACCTGCCAGTGCTTGCCTGGCAGTGGCTTCAGAGAGGACCTGGTGG  
GGAGGGAGGGCTTTCCTGTGCTGACAGCGCTCCCTCAGGAGGGCCTTGGCCTGGCACGGCTG  
TGCTCCTCCCCCTGCTCCAGCCAGAGCAGCCATCAGGCTGGAGGTGAGGATGACTTCCTGA  
AATTGGAGGGGCATGTTAAAGGGATGACTGTGCATTCCAGGGCACTGACGGAAAGCCAGGG  
CTGCAGGCAAAGCTGGACATGTGCCCTGGCCAGGAGGCCATGTTGGGCCCTCGTTTCCATT  
GCTAGTGGCCTCCTTGGGGCTCCTGTTGGCTCCTAATCCCTTAGGACTGTGGATGAGGCCAG  
ACTGGAAGAGCAGCTCCAGGTAGGGGGCCATGTTTCCAGCGGGGACCCACCAACAGAGGCC  
AGTTTCAAAGTCAGCTGAGGGGCTGAGGGGTGGGGCTCCATGGTGAATGCAGGTTGCTGCAG  
GCTCTGCCTTCTCCATGGGGTAACCACCCTCGCCTGGGCAGGGGCAGCCAAGGCTGGGAAAT  
GAGGAGGCCATGCACAGGGTGGGGCAGCTTTCTTGGGGCTTCAGTGAGAACTCTCCCAGTT  
GCCCTTGGTGGGGTTTCCACCTGGCTTTTGGCTACAGAGAGGGAAGGGAAAGCCTGAGGCCG  
GCATAAGGGGAGGCCTTGGAACCTGAGCTGCCAATGCCAGCCCTGTCCCATCTGCGGCCACG  
CTACTCGCTCCTCTCCCAACAACTCCCTTCGTGGGGACAAAAGTGACAATTGTAGGCCAGGC  
ACAGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCAAGGCGGGTGGATTACCTCCAT  
CTGTTTAGTAGAAATGGGCAAAACCCCATCTCTACTAAAAATACAAGAATTAGCTGGGCGTG  
GTGGCGTGTGCCTGTAATCCCAGCTATTTGGGAGGCTGAGGCAGGAGAATCGCTTGAGCCCG  
GGAAGCAGAGGTTGCAGTGAAGTGAAGTAGTAGTGCCACTGCAATTCAGCCTGGGTGAC  
ATAGAGAGACTCCATCTCAAAAAAA

**FIGURE 55**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45415

<subunit 1 of 1, 215 aa, 1 stop

<MW: 24326, pI: 6.32, NX(S/T): 4

MHRDAWLPRPAFSLTGLSLFFSLVPPGRSMEVTVPATLNVLNGSDARLPCTFNSCYTVNHKQ  
FSLNWTYQECNNCSEEMFLQFRMKIINLKLERFQDRVEFSGNPSKYDVSVMRLRVQPEDEGI  
YNCYIMNPDPDRHRGHGKIHLLQVLMEEPPERDSTVAVIVGASVGGFLAVVILVLMVVKCVRRK  
KEQKLSTDDLKTEEEGKTDGEGNPDDGAK

**Important features:**

**Signal peptide:**

amino acids 1-20

**Transmembrane domain:**

amino acids 161-179

**Immunoglobulin-like fold:**

amino acids 83-127

**N-glycosylation sites.**

amino acids 42-45, 66-69 and 74-77

**FIGURE 56**

GTTGTATATGTCCTGAAGTACATCCGTGCATTTTTTTTAGCATCCAACCATCCTCCCTTGTA  
GTTCTCGCCCCCTCAAATCACCTTCTCCTTAGCCACCCNACTAACATCTCAGTCTCTGAA  
AATGCACAGAGATGCCTGGCTACCTCGCCCTGCCTTCAGCCTCACGGGGCTCAGTCTCTTTT  
TCTCTTTGGTGCCACCAGGACGGAGCATGGAGGTCCACAGTACCTGNCCACCCTCAACGTCC  
TCAATGGCTCTGACGCCCCGCTGCCCTGCCCTTCAACTCCTGCTACACAGTGAACCACAAAC  
AGTTCTCCCTGAACTGGACTTACCAGGAGTGCAACAAGTCTCTGAGGAGATGTTCTCCAG  
TTCCGCATGAAGATCATTAACCTGAAGCTGGAGCGGTTTCAAGACCGCGTGGAGTTCTCAGG  
GAACCCAGCAAGTACGATGTGTCTCGGTGATGCTGAGAAACGTGCAGCCGGAGGATGAGGGGA  
TTTACAAGTCTACATCATGAACCCCCC

**FIGURE 57**

TCACGGGGCTCATCTCTTTTTCTCTTTGGTGCCCAACCAGGACGGAGCATGGAGGTNCACATA  
CCTGCCACCCTCAACGTCCTCAATGGCTTTGACGCCCCGCTGCCCTGCACCTTCAACTCCNG  
CTACACAGTGAACCACAAACAGTTCTCCCTGAACTGGATTTACCAGGAGTGCAACAACTGGC  
TCTGAGGAGATGTTCCCTCCAGTTCCCGCATGGAAGATCATTTAACCTGAAAGCTGGAAGCGG  
TTTTCAAGAACCGCGTGGAAGTTTCTCAGGGAACCCAGCAAGTACGATGTGTGGTGATGC  
TGAGAAACGTGCAGCCGGAGGATGAGGGGATTTACAACTGCTACATCATGAACCCCCC

**FIGURE 58**

TGCGGCGACCGTCGTACACCATGGGCCTCCACCTCCGCCCCCTACCGTGTGGGGCTGCTCCCG  
GATGGCCTCCTGTTCTCTTGCTGCTGCTAATGCTGCTCGCGGACCCAGCGCTCCCGGCCGG  
ACGTCACCCCCCAGTGGTGTGGTCCCTGGTGATTGGGTAACCAACTGGAAGCCAAGCTGG  
ACAAGCCGACAGTGGTGCACCTCTGCTCCAAGAAGACCGAAAGCTACTTCACAATCTGG  
CTGAACCTGGAACCTGCTGCTGCCTGTCATCATTGACTGCTGGATTGACAATATCAGGCTGGT  
TTACAACAAAACATCCAGGGCCACCCAGTTTCTGATGGTGTGGATGTACGTGTCCCTGGCT  
TTGGGAAGACCTTCTCACTGGAGTTCTGGACCCAGCAAAAGCAGCGTGGGTTCCTATTTT  
CACACCATGGTGGAGAGCCTTGTGGGCTGGGGCTACACACGGGGTGAGGATGTCCGAGGGGC  
TCCCTATGACTGGCGCCGAGCCCCAAATGAAAACGGGGCCTACTTCTGGCCCTCCGCGAGA  
TGATCGAGGAGATGTACCAGCTGTATGGGGGCCCCGTGGTGTGGTTGGCCACAGTATGGGC  
AACATGTACACGCTCTACTTTCTGCAGCGGCAGCCGAGGCCTGGAAGGACAAGTATATCCG  
GGCCTTCGTGTCACTGGGTGCGCCCTGGGGGGCGTGGCCAAGACCCTGCGCGTCTGGCTT  
CAGGAGACAACAACCGGATCCAGTCATCGGGCCCCCTGAAGATCCGGGAGCAGCAGCGGTCA  
GCTGTCTCCACCAGCTGGCTGTGCCCCTACAACCTACACATGGTCACCTGAGAAGGTGTTCTG  
GCAGACACCCACAATCAACTACACACTGCGGGACTACCGCAAGTTCTTCCAGGACATCGGCT  
TTGAAGATGGCTGGCTCATGCGGCAGGACACAGAAGGGCTGGTGGAAAGCCACGATGCCACCT  
GGCGTGCAGCTGCACTGCCTCTATGGTACTGGCGTCCCCACACCAGACTCCTTCTACTATGA  
GAGCTTCCCTGACCGTGACCCTAAAATCTGCTTTGGTGACGGCGATGGTACTGTGAACCTGA  
AGATGCCCCGAGTGCAGTGCAGGCCTGGCAGAGCCGCCAGGAGCACCAAGTGTGCTGCAGGAG  
CTGCCAGGCAGCGAGCACATCGAGATGCTGGCCAACGCCACCACCTGGCCTATCTGAAACG  
TGTGCTCCTTGGGGCCCTGACTCCTGTGCCACAGGACTCCTGTGGCTCGGGCGTGGACCTGCT  
GTTGGCCTCTGGGGCTGTGATGGCCACGCGTTTTGCAAAGTTTGTGACTCACCATTCAAGG  
CCCCGAGTCTTGGACTGTGAAGCATCTGCCATGGGGAAGTGTGTTGTTATCCTTTCTCTG  
TGGCAGTGAAGAAGGAAGAAATGAGAGTCTAGACTCAAGGGACACTGGATGGCAAGAATGCT  
GCTGATGGTGGAACTGCTGTGACCTTAGGACTGGCTCCACAGGGTGGACTGGCTGGGCCCTG  
GTCCAGTCCCTGCCTGGGGCCATGTGTCCCCCTATTCTGTGGGCTTTTCATACTTGCCCTA  
CTGGGCCCTGGCCCCGAGCCTTCTATGAGGGATGTTACTGGGCTGTGGTCTGTACCCAG  
AGGTCCAGGGATCGGCTCCTGGCCCCCTCGGGTGACCTTCCCACACACCAGCCACAGATAG  
GCCTGCCACTGGTCATGGGTAGCTAGAGCTGCTGGCTTCCCTGTGGCTTAGCTGGTGGCCAG  
CCTGACTGGCTTCTGGGCGAGCCTAGTAGCTCCTGCAGGCAGGGGCAGTTTGTGCGTTCT  
TCGTGGTTCCCAGGCCCTGGGACATCTCACTCCACTCCTACCTCCCTTACCACCAGGAGCAT  
TCAAGCTCTGGATTGGGCAGCAGATGTGCCCCAGTCCCGCAGGCTGTGTTCCAGGGGCCCT  
GATTTCTCGGATGTGCTATTGGCCCCAGGACTGAAGCTGCCTCCCTTACCCTGGGACTGT  
GGTTCCAAGGATGAGAGCAGGGGTGGAGCCATGGCCTTCTGGGAACCTATGGAGAAAGGGA  
ATCCAAGGAAGCAGCAAGGCTGCTCGCAGCTTCCCTGAGCTGCACCTCTTGCTAACCCAC  
CATCACACTGCCACCCTGCCCTAGGGTCTCACTAGTACCAAGTGGGTCAGCACAGGGCTGAG  
GATGGGGCTCCTATCCACCCTGGCCAGCACCCAGCTTAGTGCTGGGACTAGCCAGAACTT  
GAATGGGACCCTGAGAGAGCCAGGGGTCCCCTGAGGCCCCCTAGGGGCTTTCTGTCTGCC  
CAGGGTGTCCATGGATCTCCCTGTGGCAGCAGGCATGGAGAGTCAGGGCTGCCTTCATGGC  
AGTAGGCTCTAAGTGGGTGACTGGCCACAGGCCGAGAAAAGGGTACAGCCTCTAGGTGGGGT  
TCCCAAAGACGCCTTCAAGCTGGACTGAGCTGCTCTCCACAGGGTTTCTGTGCAGCTGGAT  
TTTCTCTGTTGCATACATGCCTGGCATCTGTCTCCCCTGTTCTGAGTGGCCCCACATGGG  
GCTCTGAGCAGGCTGTATCTGGATTCTGGCAATAAAAGTACTCTGGATGCTGTAAAAA  
AAAAA



**FIGURE 59**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44189  
><subunit 1 of 1, 412 aa, 1 stop  
><MW: 46658, pI: 6.65, NX(S/T): 4  
MGLHLRPYRVGLLPDGLLFLLLLLLMLLADPALPAGRHPVVLVPGDLGNQLEAKLDKPTVVH  
YLCSKKTESYFTIWLNLLELLLPVIIDCWIDNIRLVYNKTSRATQFPDGVDRVPGFGKTFSL  
EFLDPSKSSVGSYFHTMVESLVGWGYTRGEDVRGAPYDWRRAPNENGPYFLALREMIEMYQ  
LYGGPVVLVAHSMGMYTLYFLQRQPQAWKDKYIRAFVSLGAPWGGVAKTLRVLASGDNRI  
PVIGPLKIREQORSVSTSWLLPYNYTWSPEKVVFVQTPTINYTLRDYRKFFQDIGFEDGWL  
RQDTEGLVEATMPPGVQLHCLYGTGVPTPDSFYYESFPDRDPKICFGDGDGTVNLKSALQCQ  
AWQSRQEHQVLLQELPGSEHIEMLANATTLAYLKRVLLGP

**Important features:****Signal peptide:**

amino acids 1-28

**Potential lipid substrate binding site:**

amino acids 147-164

**N-glycosylation sites.**

amino acids 99-102, 273-276, 289-292 and 398-401

**Lipases, serine proteins**

amino acids 189-201

**Beta-transducin family Trp-Asp repeat**

amino acids 353-365



**FIGURE 61**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48304

<subunit 1 of 1, 224 aa, 1 stop

<MW: 24810, pI: 4.75, NX(S/T): 1

MESGAYGAAGAGGSFDLRRFLTQPQVVARAVCLVFALIVFSCIYGEYSNAHESKQMYCVFN  
RNEDACRYGSAIGVLAFLASAFFLVVDAYFPQISNATDRKYL VIGDLLFSALWTF LWFGFC  
FLTNQWAVTNPKDVLVGADSVRAAITFSFFSIFSWGVLASLAYQRYKAGVDDFIQNYVDPTP  
DPNTAYASYPGASVDNYQPPFTQNAETTEGYQPPPVY

**Important features:**

**Type II Transmembrane domain:**

amino acids 24-43

**Other transmembrane domains:**

amino acids 74-90, 108-126 and 145-161

**N-glycosylation site.**

amino acids 97-100

**FIGURE 62**

GAGCCACCTACCCTGCTCCGAGGCCAGGCCTGCAGGGCCTCATCGGCCAGAGGGTGATCAGT  
GAGCAGAAGGATGCCCCGTGGCCGAGGCCCCCCAGGTGGCTGGCGGGCAGGGGGACGGAGGTG  
ATGGCGAGGAAGCGGAGCCAGAGGGGATGTTCAAGGCCTGTGAGGACTCCAAGAGAAAAGCC  
CGGGGCTACCTCCGCCTGGTGCCCCCTGTTTGTGCTGCTGGCCCTGCTCGTGCTGGCTTCGGC  
GGGGGTGCTACTCTGGTATTTCTAGGGTACAAGGCGGAGGTGATGGTCAGCCAGGTGTACT  
CAGGCAGTCTGCGTGTACTCAATCGCCACTTCTCCAGGATCTTACCCGCCGGGAATCTAGT  
GCCTTCCGCGAGTGAACCCGCCAAAGCCCAGAAGATGCTCAAGGAGCTCATCACCAGCACCCG  
CCTGGGAACCTTACTACAACTCCAGCTCCGCTCTATTCTTTGGGGAGGGACCCCTCACCTGCT  
TCTTCTGGTTTCAATTCTCCAAATCCCCGAGCACCGCGCTGATGCTGAGCCCCGAGGTGGTG  
CAGGCACTGCTGGTGGAGGAGCTGCTGTCCACAGTCAACAGCTCGGCTGCCGTCCCCTACAG  
GGCCGAGTACGAAGTGGACCCCGAGGGCCTAGTGATCCTGGAAGCCAGTGTGAAGACATAG  
CTGCATTGAATTCCACGCTGGGTGTTGTTACCGCTACAGCTACGTGGGCCAGGGCCAGCTCCTC  
CGGCTGAAGGGGCCTGACCACCTGGCCTCCAGCTGCCTGTGGCACCTGCAGGGCCCCAAGGA  
CCTCATGCTCAAACCTCCGGCTGGAGTGGACGCTGGCAGAGTGC CGGGACCGACTGGCCATGT  
ATGACGTGGCCGGGCCCCCTGGAGAAGAGGCTCATCACCTCGGTGTACGGCTGCAGCCGCCAG  
GAGCCCGTGGTGGAGGTTCTGGCGTGGGGGCCATCATGGCGGTGCTGGAAGAAGGGCCT  
GCACAGCTACTACGACCCCTTCGTGCTCTCCGTGCAGCCGTTGGTCTTCCAGGCCTGTGAAG  
TGAACCTGACGCTGGACAACAGGCTCGACTCCAGGGCGTCTCAGCACCCCGTACTTCCCC  
AGCTACTACTCGCCCCAAACCCACTGCTCCTGGCACCTCACGGTGCCCTCTCTGGACTACGG  
CTTGGCCCTCTGGTTTGATGCTATGCACTGAGGAGGCAGAAAGTATGATTTGCCGTGCACCC  
AGGGCCAGTGGACGATCCAGAACAGGAGGCTGTGTGGCTTGCGCATCCTGCAGCCCTACGCC  
GAGAGGATCCCCGTGGTGGCCACGGCCGGGATCACCATCAACTTCACCTCCCAGATCTCCCT  
CACCGGGCCCGGTGTGCGGGTGCACTATGGCTTGTAACAACAGTCCGACCCCTGCCCTGGAG  
AGTTCTCTGTTCTGTGAATGGACTCTGTGTCCCTGCCTGTGATGGGGTCAAGGACTGCCCC  
AACGGCCCTGGATGAGAGAACTGCGTTTGCAGAGCCACATTCAGTGCAAAGAGGACAGCAC  
ATGCATCTCACTGCCCCAAGGTCTGTGATGGGCAGCCTGATTGTCTCAACGGCAGCGATGAAG  
AGCAGTGCCAGGAAGGGGTGCCATGTGGGACATTCACCTTCAGTGTGAGGACCGGAGCTGC  
GTGAAGAAGCCCAACCCGCGAGTGTGATGGGCGGCCGACTGCAGGGACCGCTCGGATGAGGA  
GCACTGTGACTGTGGCCTCCAGGGCCCCCTCCAGCCGCAATTGTTGGTGGAGCTGTGTCTCCG  
AGGGTGAGTGGCCATGGCAGGCCAGCCTCCAGGTTCCGGGTCCACACATCTGTGGGGGGGCC  
CTCATCGCTGACCGCTGGGTGATAACAGCTGCCCCACTGCTTCCAGGAGGACAGCATGGCCTC  
CACGGTGCTGTGGACCGTGTTCCTGGGCAAGGTGTGGCAGAACTCGCGCTGGCCTGGAGAGG  
TGTCCTTCAAGGTGAGCCGCTGCTCCTGCACCCGTACCACGAAGAGGACAGCCATGACTAC  
GACGTGGCGCTGCTGCAGCTCGACCACCCGGTGGTGGCTCGGCCGCGCTGCGCCCGCTGCTG  
CCTGCCCGCGCGCTCCCACTTCTTCGAGCCCGGCTGCACTGCTGGATTACGGGCTGGGGCG  
CCTTGCGCGAGGGCGGGCCCCATCAGCAACGCTCTGCAGAAAGTGGATGTGCAGTTGATCCCA  
CAGGACCTGTGCAGCGAGGCCTATCGCTACCAGGTGACGCCACGCATGCTGTGTGCCGGCTA  
CCGCAAGGGCAAGAAGGATGCCTGTGAGGGTGAAGTCAAGGTGGTCCGCTGGTGTGCAAGGCAC  
TCAGTGGCCGCTGGTTCTGGCGGGGCTGGTCAAGTGGGGCCTGGGCTGTGGCCGGCCTAAC  
TACTTCGGCGTCTACACCCGCATCAGAGTGTGATCAGCTGGATCCAGCAAGTGGTGACCTG  
AGGAACCTGCCCCCTGCAAAGCAGGGCCCACTCCTGGACTCAGAGAGCCAGGGCAACTGC  
CAAGCAGGGGGACAAGTATTCTGGCGGGGGTGGGGGAGAGAGCAGGCCCTGTGGTGGCAGG  
AGGTGGCATCTTGTCTCGTCCCTGATGTCTGCTCCAGTGTGTCAGGAGGATGGAGAAGTGC  
CAGCAGCTGGGGGTCAAGACGTCCCCTGAGGACCCAGGCCACACCCAGCCCTTCTGCCTCC  
CAATTCTCTCTCCTCCGTCCCCTTCTCCACTGCTGCCTAATGCAAGGCAGTGGCTCAGCAG  
CAAGAATGCTGGTTCTACATCCCGAGGAGTGTCTGAGGTGCGCCCCACTCTGTACAGAGGCT  
GTTTGGGCAGCCTTGCCCTCCAGAGAGCAGATTCCAGCTTCGGAAGCCCCCTGGTCTAACTGG  
GATCTGGGAATGGAAGGTGCTCCCATCGGAGGGGACCCCTCAGAGCCCTGGAGACTGCCAGGT  
GGGCTGCTGCCACTGTAAGCCAAAAGGTGGGGAAGTCTGACTCCAGGGTCTTGCCCCAC  
CCCTGCCCTGCCACCTGGGCCCTCACAGCCAGACCTCACTGGGAGGTGAGCTCAGCTGCCC  
TTTGAATAAAGCTGCCTGATCAAAAAAAAAAAAAAAAAAAAAA

**FIGURE 63**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA49152  
><subunit 1 of 1, 802 aa, 1 stop  
><MW: 88846, pI: 6.41, NX(S/T): 7  
MPVAEAPQVAGGQGDGGDGEAEPEGMFKACEDSKRKARGYLRLVPLFVLLALLVLASAGVL  
LWYFLGYKAEVMVSQVYSGSLRVLNRHFSQDLTRRESSAFRSETAKAQKMLKELITSTRLGT  
YYNSSSVYSFGEGPLTCFFWFILQIPEHRRMLLSPEVVQALLVEELLSTVNSSAAVPYRAEY  
EVDPEGLVILEASVKDIAALNSTLGCYRYSYVGQGVRLRLKGPDLHASSCLWHLQGPDKLML  
KLRLEWTLAECRDLAMYDVAGPLEKRLITSVYGCSRQEPVVEVLASGAIMAVVWKKGLHSY  
YDPFVLSVQPVVFQACEVNLTLNRLDSQGVLSPTYFPSYSPQTHCSWHLTPVPSLDYGLAL  
WFDAYALRRQKYDLPCTQGQWTIQNRRLCGLRIQPYAERIPVVATAGITINFTSQISLTGP  
GVRVHYGLYNQSDPCPGEFLLCSVNLGCVLPACDGVKDCPNGLDERNCVCRATFQCKEDSTCIS  
LPKVCDDGQPDCLNGSDEEQCQEGVPCGTFTFQCEDRSCVKPNPQCDGRPDGRDGSDEEHCD  
CGLQGPPSSRIVGGAVSSEGEWQASLQVRGRHICGGALIADRWVITAHCFOEDSMASVTL  
WTVFLGKVWQNSRWPGEVSKVSRLLLHPYHEEDSHDYDVALLQLDHPVVRSAAVRPVCLPA  
RSHFFEPGLHCWITGWGALREGGPISNALQKVDVQLIPQDLCSEAYRYQVTPRMLCAGYRKG  
KKDACQGDGGPLVCKALSGRWFLAGLVSWGLGCGRPNYFGVYTRITGVISWQQVVT

**Important features:****Type II transmembrane domain:**

amino acids 46-67

**Serine proteases, trypsin family, histidine active site.**

amino acids 604-609

**N-glycosylation sites.**amino acids 127-130, 175-178, 207-210, 329-332, 424-427, 444-447  
and 509-512**Kringle domains.**

amino acids 746-758 and 592-609

**Homologous region to Kallikrein Light Chain:**

amino acids 568-779

**Homologous region to Low-density lipoprotein receptor:**

amino acids 451-567

**FIGURE 64**

GCACCCAGGGCCAGTGGACGATCCAGAACAGGAGGCTGTGTGGCTTGCGCATCCTGCAGCCC  
TACGCCGAGAGGATCCCCGTGGTGGCCACGGCCGGGATCACCATCAACTTCACCTCCCAGAT  
CTCCCTCACCGGGCCCGGTGTGCGGGTGCACTATGGCTTGTACAACCAAGTCGGACCCCTGCC  
CTGGAGAGTTCTCTGTTCTGTGAATGGACTCTGTGTCCCTGCCTGTGATGGGGTCAAGGAC  
TGCCCCAACGGCCTGGATGAGAGAACTGCGTTTGCAGAGCCACATTCCAGTGCAAAGAGGA  
CAGCACATGCATCTCACTGCCCAAGGTCTGTGATGGGCAGCCTGATTGTCTCAACGGCAGCG  
ATGAAGAGCAGTGCCAGGAAGGGGTGCCATGTGGGACATTACCTTCCAGTGTGAGGACCGG  
AGCTGCGTGAAGAAGCCCAACCCGCAGTGTGATGGGCGGCCCCGACTGCAGGGACGGCTCGGA  
TGAGGAGCACTGTGACTGTGGCCTCCAGGGCCCCCTCCAGCCGCATTGTTGGTGGAGCTGTGT  
CCTCCGAGGGTGAGTGGCCATGGCAGGCCAGCCTCCAGGTTGCGGGTGCACACATCTGTGGG  
GGGGCCCTCATCGCTGACCGCTGGGTGATAACAGCTGCCCACTGCTTCCAGGAGGACAGCAT  
GGCCTCCACGGTGCTGTGGACCGTGTTCTTGGGCAAGGTGTGGCAGAACTCGCGCTGGCCTG  
GAGAGGTGTCCTTCAAGGTGAGCCGCCTGCTCCTGCACCCGTACCACGAAGAGGACAGCCAT  
GACTACGACGTGGCGCTGCTGCAGCTCGACCACCCGGTGGTGGCTCGGCCGCCGTGCGCCC  
CGTCTGCCTGCCCGCGCGCTCCCACTTCTTCGAGCCCGGCCTGCACTGCTGGATTACGGGCT  
GGGGCGCCTTGCGCGAGGGCGGCCCCATCAGCAACGCTCTGCAGAAAGTGGATGTGCAGTTG  
ATCCACAGGACCTGTGCAGCGAGGCCTATCGCTACCAGGTGACGCCACGCATGCTGTGTGC  
CGGCTACCGCAAGGGCAAGAAGGATGCCTGTGAGGGTGAATCAGGTGGTCCGCTGGTGTGCA  
AGGCACTCAGTGGCCGCTGGTTCTTGGCGGGGCTGGTCAGCTGGGGCCTGGGCTGTGGCCGG  
CCTAACTACTTCGGCGTCTACACCCGCATCACAGGTGTGATCAGCTGGATCCAGCAAGTGGT  
GACCTGAGGAACTGCCCCCTGCAAAGCAGGGCCACCTCCTGGACTCAGAGAGCCCAGGGC  
AACTGCCAAGCAGGGGGACAAGTAT

**FIGURE 65**

GGACGAGGGCAGATCTCGTTCTGGGGCAAGCCGTTGACACTCGCTCCCTGCCACCGCCCGGG  
CTCCGTGCCGCCAAGTTTTTCATTTTCCACCTTCTCTGCCTCCAGTCCCCCAGCCCCCTGGCCG  
AGAGAAGGGTCTTACCGGCCGGGATTGCTGGAAACACCAAGAGGTGGTTTTTGTTTTTTAAA  
ACTTCTGTTTCTTGGGAGGGGGTGTGGCGGGGCAGGATGAGCAACTCCGTTCCCTCTGCTCTG  
TTTCTGGAGCCTCTGCTATTGCTTTGCTGCGGGGAGCCCCGTACCTTTTGGTCCAGAGGGAC  
GGCTGGAAGATAAGCTCCACAAACCCAAAGCTACACAGACTGAGGTCAAACCATCTGTGAGG  
TTTAACCTCCGCACCTCCAAGGACCCAGAGCATGAAGGATGCTACCTCTCCGTGCGCCACAG  
CCAGCCCTTAGAAGACTGCAGTTTCAACATGACAGCTAAAACCTTTTTTCATCATTACGGAT  
GGACGATGAGCGGTATCTTTGAAAACCTGGCTGCACAAACTCGTGTGAGCCCTGCACACAAGA  
GAGAAAGACGCCAATGTAGTTGTGGTTGACTGGCTCCCCCTGGCCCACCAGCTTTACACGGA  
TGCGGTCAATAATACCAGGGTGGTGGGACACAGCATTGCCAGGATGCTCGACTGGCTGCAGG  
AGAAGGACGATTTTTTCTCTCGGGAATGTCCACTTGATCGGCTACAGCCTCGGAGCGCACGTG  
GCCGGGTATGCAGGCAACTTCGTGAAAGGAACGGTGGGCCGAATCACAGGTTTGGATCCTGC  
CGGGCCCATGTTTGAAGGGGCCGACATCCACAAGAGGCTCTCTCCGGACGATGCAGATTTTG  
TGGATGTCTCCACACCTACACGCGTTCCTTCGGCTTGAGCATTGGTATTAGATGCCTGTG  
GGCCACATTGACATCTACCCCAATGGGGGTGACTTCCAGCCAGGCTGTGGACTCAACGATGT  
CTTGGGATCAATTGCATATGGAACAATCACAGAGGTGGTAAAATGTGAGCATGAGCGAGCCG  
TCCACCTCTTTGTTGACTCTCTGGTGAATCAGGACAAGCCGAGTTTTGCCTTCCAGTGCCT  
GACTCCAATCGCTTCAAAAAGGGGATCTGTCTGAGCTGCCGCAAGAACCGTTGTAATAGCAT  
TGGCTACAATGCCAAGAAAATGAGGAACAAGAGGAACAGCAAAATGTACCTAAAAAGCCGGG  
CAGGCATGCCTTTCAGAGGTAACCTTCAGTCCCTGGAGTGTCCCTGAGGAAGGCCCTTAATA  
CCTCCTTCTTAATACCATGCTGCAGAGCAGGGCACATCCTAGCCCAGGAGAAGTGGCCAGCA  
CAATCCAATCAAATCGTTGCAAATCAGATTACACTGTGCATGTCTAGGAAAGGGAATCTTT  
ACAAAATAAACAGTGTGGACCCCTAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA  
AAAAAAAAAAAAAAAAAAAAA

**FIGURE 66**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA49646

><subunit 1 of 1, 354 aa, 1 stop

><MW: 39362, pI: 8.35, NX(S/T): 2

MSNSVPLLCLFWSLCYCFAGSPVPFGPEGRLEDKLHKPKATQTEVKPSVRFNLRRTSKDPEHE  
GCYLSVGHSQPLEDCSFNMTAKTFFIIHGWTMSGIFENWLHKLVSALHTREKDANVVVDWL  
PLAHQLYTDAVNNTRVVGHSIARMLDWLQEKDDFSLGNVHLIGYSLGAHVAGYAGNFVKGTV  
GRITGLDPAGPMFEGADIAKRLSPDDADFVDVLHTYTRSFGLSIGIQMPVGHIDIYPNGGDF  
QPGCGLNDVLGSIAYGTITEVVKCEHERAVHLFVDSLVDKPSFAFQCTDSNRFKKGICLS  
CRKNRCNSIGYNAKKMRNKRNSKMYLKTRAGMPFRGNLQSLECP

**Important features:**

**Signal peptide:**

amino acids 1-16

**Lipases, serine active site.**

amino acids 163-172

**N-glycosylation sites.**

amino acids 80-83 and 136-139



**FIGURE 67**

CGGACGCGTGGGCGGACGCGTGGGCCTGGGCAAGGGCCGGGGCGCCGGGCGGAGCCACCTCT  
TCCCTCCCCGCTTCCCTGTCGCGCTCCGCTGGCTGGACGCGCTGGAGGAGTGGAGCAGCA  
CCCGGGCGGCCCTGGGGGCTGACAGTCGGCAAAGTTTGGCCCGAAGAGGAAGTGGTCTCAAA  
CCCCGGCAGGTGGCGACCAGGCCAGACCAGGGGCGCTCGCTGCCTGCGGGCGGGCTGTAGGC  
GAGGGCGCGCCCCAGTGGCGAGACCCGGGGCTTCAGGAGCCGGCCCCGGGAGAGAAGAGTGC  
GGCGGCGGACGGAGAAAACAACCTCCAAAGTTGGCGAAAGGCACCGCCCCCTACTCCCGGGCTG  
CCGCCGCTCCCCGCCCCCAGCCCTGGCATCCAGAGTACGGGTGAGCCCCGGGCCATGGAGC  
CCCCCTGGGGAGGCGGCACCAGGGAGCCTGGGCGCCCCGGGGCTCCGCCGCGACCCCATCGGG  
TAGACCACAGAAGCTCCGGGACCCTTCCGGCACCTCTGGACAGCCCAGGATGCTGTTGGCCA  
CCCTCCTCCTCCTCCTCCTTGGAGGCGCTCTGGCCCATCCAGACCGGATTATTTTTCCAAAT  
CATGCTTGTGAGGACCCCCCAGCAGTGCTCTTAGAAGTGCAGGGCACCTTACAGAGGCCCCCT  
GGTCCGGGACAGCCGCACCTCCCCTGCCAACTGCACCTGGCTCATCCTGGGCAGCAAGGAAC  
AGACTGTCACCATCAGGTTCCAGAAGCTACACCTGGCCTGTGGCTCAGAGCGCTTAACCCTA  
CGTCCCCCTCTCCAGCCACTGATCTCCCTGTGTGAGGCACCTCCCAGCCCTCTGCAGCTGCC  
CGGGGGCAACGTACCATCACTTACAGCTATGCTGGGGCCAGAGCACCCATGGGCCAGGGCT  
TCCTGCTCTCCTACAGCCAAGATTGGCTGATGTGCCTGCAGGAAGAGTTTCAGTGCCTGAAC  
CACCCTGTGTATCTGCTGTCCAGCGCTGTGATGGGGTTGATGCCTGTGGCGATGGCTCTGA  
TGAAGCAGGTTGCAGCTCAGACCCCTTCCCTGGCCTGACCCCAAGACCCGTCCTCCTGTC  
CTTGCAATGTCACCTTGGAGGACTTCTATGGGGTCTTCTCCTCTCCTGGATATACACACCTA  
GCCTCAGTCTCCACCCCCAGTCTGCCATTGGCTGCTGGACCCCATGATGGCCGGCGGGCT  
GGCCGTGCGCTTACAGCCCTGGACTTGGGCTTGGAGATGCAGTGCATGTGTATGACGGCC  
CTGGGCCCCCTGAGAGCTCCCGACTACTGCGTAGTCTACCCACTTCAGCAATGGCAAGGCT  
GTCACCTGTGGAGACACTGTCTGGCCAGGCTGTGTGCTCCTACACACAGTTGCTTGGAGCAA  
TGGTCTGTGGCTTCAATGCCACCTACCATGTGGGGGCTATTGCTTGCCTTGGGACAGACCT  
GTGGCTTAGGCTCTGGCCTGGGAGCTGGCGAAGGCCTAGGTGAGCGCTGCTACAGTGAGGCA  
CAGCGCTGTGACGGCTCATGGGACTGTGCTGACGGCACAGATGAGGAGGACTGCCAGGCTG  
CCCACCTGGACACTTCCCTGTGGGGCTGCTGGCACCTCTGGTGCCACAGCTGCTACCTGCTG  
CTGCTGACCGCTGCAACTACCAGACTTTCTGTGCTGATGGAGCAGATGAGAGACGCTGTGCG  
CATTGCCAGCTGGCAATTTCCGATGCCGGGACGAGAAGTCCGTGTATGAGACGTTGGGTGTG  
CGATGGGCAGCCAGACTGTGCGGACGGCAGTGATGAGTGGGACTGCTCCTATGTTCTGCCCC  
GCAAGGTCATTACAGCTGCAGTCATTGGCAGCCTAGTGTGCGGCCTGCTCCTGGTCATCGCC  
CTGGGCTGCACCTGCAAGCTCTATGCCATTGCGACCCAGGAGTACAGCATCTTTGCCCCCT  
CTCCCGGATGGAGGCTGAGATTGTGACAGCAGGACCCCCCTTCTACGGGCAGCTCATTG  
CCCAGGGTGCCATCCCACCTGTAGAAGACTTTCTACAGAGAATCCTAATGATAACTCAGTG  
CTGGGCAACCTGCGTTCTCTGCTACAGATCTTACGCCAGGATATGACTCCAGGAGGTGGCCC  
AGGTGCCCCGCGTCTGTCAGCGGGGCGCTTGATGCGACGCTGGTACGCGCTCTCCGCCGCT  
GGGGCTTGCTCCCTCGAACCAACACCCCGGCTCGGGCCTCTGAGGCCAGATCCCAGGTCACA  
CCTTCTGCTGCTCCCTTGGAGCCCTAGATGGTGGCACAGGTCCAGCCCGTGAGGGCGGGGC  
AGTGGGTGGGCAAGATGGGGAGCAGGCACCCCCACTGCCCATCAAGGCTCCCCCTCCATCTG  
CTAGCACGTCTCCAGCCCCACTACTGTCCCTGAAGCCCCAGGGCCACTGCCCTCACTGCCC  
CTAGAGCCATCACTATTGTCTGGAGTGGTGCAGGCCCTGCGAGGCCGCTGTGCCCAGCCT  
GGGGCCCCCAGGACCAACCCGGAGCCCCCTGGACCCACACAGCAGTCTTGCCCTGGAAG  
ATGAGGACGATGTGCTACTGGTGGCACTGGCTGAGCCGGGGGTGTGGGTAGCTGAGGCAGAG  
GATGAGCCACTGCTTACCTGAGGGGACCTGGGGGCTCTACTGAGGCCTCTCCCCTGCGGGCT  
CTACTCATAGTGGCACAACCTTTTAGAGGTGGGTGAGCCTCCCCCTCCACCACTTCTTCCCT  
GTCCCTGGATTTCAGGGACTTGGTGGGCCTCCCGTTGACCCTATGTAGCTGCTATAAAGTTA  
AGTGTCCCTCAGGCAGGGAGAGGGCTCACAGAGTCTCCTCTGTACGTGGCCATGGCCAGACA  
CCCCAGTCCCTTACCACCACCTGCTCCCCACGCCACCACCATTTGGGTGGCTGTTTTTAA  
AAGTAAAGTTCTTAGAGGATCATAGGTCTGGACACTCCATCCTTGCCAAACCTTACCCAAA  
AGTGGCCTTAAGCACCAGGAATGCCAATTAAGTAGAGACCTCCAGCCCCAAGGGGAGGATT  
TGGGCAGAACCTGAGGTTTTGCCATCCACAATCCCTCCTACAGGGCCTGGCTCACAAAAGA  
GTGCAACAAATGCTTCTATTCCATAGCTACGGCATGTCTCAGTAAGTTGAGGTCAAAAATAA  
AGGAATCATACATCTC

**FIGURE 68**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA49631

<subunit 1 of 1, 713 aa, 1 stop

<MW: 76193, pI: 5.42, NX(S/T): 4

MLLATLLLLLLGGALAHDPRIIFPNHACEDPPAVLLEVOGTLQRPLVRDSRTSPANCTWLIL  
GSKEQTVTIRFQKLHLACGSERLTLRSPLQPLISLCEAPPSPLQLPGGNVTITYSYAGARAP  
MGQGFLLSYSQDWLMCLQEEFQCLNHRCSVSAVQRCDGVDACGDGSDEAGCSSDPFPGLTFRP  
VPSLPCNVTLEDFYGVFSSPGYTHLASVSHPOQSCHWLLDPHDGRRRLAVRFTALDLGFGDAVH  
VYDGPGPPESSRLLRSLTHFSNGKAVTVETLSGQAVVSYHTVAWSNGRGFNATYHVRGYCLP  
WDRPCGLGSGLGAGEGLGERCYSEAQRCDGSWDCADGTDEEDCPGCPPGHFPCGAAGTSGAT  
ACYLPADRCNYQTFCADGADERRCRHCQPGNFRRCRDEKCVYETWVCDGQPD CADGSDEWDCS  
YVLPRKVITA AVIGSLVCGLLLVIALGCTCKLYAIRTQEYSIFAPLSRMEAEIVQQQAPPSY  
GQLIAQGAIPPVEDFPTENPNDNSVLGNLRSLLQILRQDMTPGGGPGARRRQGRMLRRLVR  
RLRRWGLLPRTNTPARASEARSQVTPSAAPLEALDGGTGPAREGGAVGGQDGEQAPPLPIKA  
PLPSASTSPAPTTVPEAPGPLPSLPLEPSLLSGVVQALRGRLLP SLGPPGPTRSPPGPHTAV  
LALEDEDDVLLVPLAEPGVWVAEAEDEPLLT

**Important features:**

**Signal peptide:**

amino acids 1-16

**Transmembrane domain:**

amino acids 442-462

**LDL-receptor class A (LDLRA) domain proteins**

amino acids 411-431, 152-171, 331-350 and 374-393

**FIGURE 69**

CGAGCTGGGCGAGAAGTAGGGGAGGGCGGTGCTCCGCCGCGGTGGCGGTTGCTATCGCTTCG  
CAGAACCTACTCAGGCAGCCAGCTGAGAAGAGTTGAGGGAAAGTGCTGCTGCTGGGTCTGCA  
GACGCGATGGATAACGTGCAGCCGAAAATAAAACATCGCCCCTTCTGCTTCAGTGTGAAAGG  
CCACGTGAAGATGCTGCGGCTGGCACTAACTGTGACATCTATGACCTTTTTTATCATCGCAC  
AAGCCCCCTGAACCATATATTGTTATCACTGGATTTGAAGTCACCGTTATCTTATTTTTCATA  
CTTTTATATGTACTCAGACTTGATCGATTAATGAAGTGGTTATTTTGGCCTTTGCTTGATAT  
TATCAACTCACTGGTAACAACAGTATTCATGCTCATCGTATCTGTGTTGGCACTGATACCAG  
AAACCACAACATTGACAGTTGGTGGAGGGGTGTTTGCACTTGTGACAGCAGTATGCTGTCTT  
GCCGACGGGGCCCTTATTTACCGGAAGCTTCTGTTCAATCCCAGCGGTCCTTACCAGAAAAA  
GCCTGTGCATGAAAAAAAGAAGTTTTGTAATTTTATATTACTTTTGTAGTTTGATACTAAGT  
ATTAAACATATTTCTGTATTCTTCAAAAAAAAAAAAAAAAAAAAA

**FIGURE 70**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA49645

><subunit 1 of 1, 152 aa, 1 stop

><MW: 17170, pI: 9.62, NX(S/T): 1

MDNVQPKIKHRPFCFSVKGHVKMLRLALTVTSMTEFFIIAQAPEPYIVITGFEVTVILFFILL  
YVLRDLRLMKWLFWPLLDIINSLVTTVFMLIVSVLALIPETTTTLTVGGGVFALVTAVCCLAD  
GALIYRKLLFNPSGPYQKKPVHEKKEVL

**Important features:**

**Potential type II transmembrane domain:**

amino acids 26-42

**Other potential transmembrane domain:**

amino acids 44-65, 81-101 and 109-129

**Leucine zipper pattern**

amino acids 78-99 and 85-106

**N-myristoylation site.**

amino acids 110-115

**Ribonucleotide reductase large subunit protein**

amino acids 116-127

**FIGURE 71**

GGGCGAGAAGTAGGGGAGGGCGTGTTCCGCCGCGGTGGCGGTTGCTATCGTTTTGCAGAACC  
TACTCAGGCAGCCAGNTGAGAAGAGTTGAGGGAAAGTGCTGCTGCTGGGTCTGCAGACGCGA  
TGGATAACGTGCAGCCGAAAATAAAACATCGCCCCCTTCTGCTTCAGTGTGAAAGGCCACGTG  
AAGATGCTGCGGCTGGCACTAACTGNGACATCTATGACCTTTTTTATNATCGCACAAAGCCCC  
TGAACCATATATTGTTATCACTGGATTGGAAGTCACCGTTATCTTATTTTTTCATACTTTTAT  
ATGTACTCAGACTTGATCGATTAATGAAGTGGTTATTTTGGCCTTTGCTTGATATTATCAAC  
TCACTGGTAACAACAGTATTCATGCTCATCGTATCTGTGTTGGCACTGATACCAGAAACCAC  
AACATTGACAGTTGGTGGAGGGGTGTTTGCACTTGTGACAGCAGTATGCTGTNTTGCCGAC

**FIGURE 72**

CAGCCCCGCGCGCCGGCCGAGTCGCTGAGCCGCGGCTGCCGGACGGGACGGGACCGGCTAGG  
CTGGGCGCGCCCCCGGGCCCCGCGTGGGCATGGGCGCACTGGCCCCGGGCGCTGCTGCTGC  
CTCTGCTGGCCCAGTGGCTCCTGCGCGCCGCCCCGGAGCTGGCCCCCGCGCCCTTCACGCTG  
CCCCCTCCGGGTGGCCGCGGCCACGAACCGCGTAGTTGCGCCACCCCGGGACCCGGGACCCC  
TGCCGAGCGCCACGCCGACGGCTTGGCGCTCGCCCTGGAGCCTGCCCTGGCGTCCCCCGCGG  
GCGCCGCCAACTTCTTGCCATGGTAGACAACCTGCAGGGGGACTCTGGCCGCGGCTACTAC  
CTGGAGATGCTGATCGGGACCCCCCGCAGAAGCTACAGATTCTCGTTGACACTGGAAGCAG  
TAACTTTGCCGTGGCAGGAACCCCGCACTCCTACATAGACACGTACTTTGACACAGAGAGGT  
CTAGCACATAACCGCTCCAAGGGCTTTGACGTCACAGTGAAGTACACACAAGGAAGCTGGACG  
GGCTTCGTTGGGGAAGACCTCGTCACCATCCCCAAAGGCTTCAATACTTCTTTTCTTGTCAA  
CATTGCCACTATTTTTGAATCAGAGAATTTCTTTTGCCTGGGATTAAATGGAATGGAATAC  
TTGGCCTAGCTTATGCCACACTTGCCAAGCCATCAAGTTCTCTGGAGACCTTCTTCGACTCC  
CTGGTGACACAAGCAAACATCCCCAACGTTTTCTCCATGCAGATGTGTGGAGCCGGCTTGCC  
CGTTGCTGGATCTGGGACCAACGGAGGTAGTCTTGCTTGGGTGGAATTGAACCAAGTTTGT  
ATAAAGGAGACATCTGGTATACCCCTATTAAGGAAGAGTGGTACTACCAGATAGAAATTCTG  
AAATTGGAATTTGGAGGCCAAAGCCTTAATCTGGACTGCAGAGAGTATAACGCAGACAAGGC  
CATCGTGGACAGTGGCACCACGCTGCTGCGCCTGCCCCAGAAGGTGTTTGATGCGGTGGTGG  
AAGCTGTGGCCCGCGCATCTCTGATTCCAGAATTCTCTGATGGTTTCTGGACTGGGTCCAG  
CTGGCGTGCTGGACGAATTCGGAACACCTTGGTCTTACTTCCCTAAAATCTCCATCTACCT  
GAGAGACGAGAACTCCAGCAGGTCAATCCGTATCACAACTCCTGCCTCAGCTTTACATTGAGC  
CCATGATGGGGGCCGGCTGAATTATGAATGTTACCGATTGGGCATTTCCCATCCACAAAT  
GCGCTGGTGATCGGTGCCACGGTGATGGAGGGCTTCTACGTCATCTTCGACAGAGCCCAGAA  
GAGGGTGGGCTTCGCAGCGAGCCCCTGTGCAGAAATTGCAGGTGCTGCAGTGTCTGAAATTT  
CCGGGCCTTTCTCAACAGAGGATGTAGCCAGCAACTGTGTCCCCGCTCAGTCTTTGAGCGAG  
CCCATTTTGTGGATTGTGTCTATGCGCTCATGAGCGTCTGTGGAGCCATCCTCCTTGCTTT  
AATCGTCCTGCTGCTGCTGCCGTTCCGGTGTGAGCGTCGCCCCGTGACCCTGAGGTCGTCA  
ATGATGAGTCCTCTCTGGTCAGACATCGCTGGAATGAATAGCCAGGCCTGACCTCAAGCAA  
CCATGAACTCAGCTATTAAGAAAATCACATTTCCAGGGCAGCAGCCGGGATCGATGGTGGCG  
CTTTCTCCTGTGCCCACCCGTCTTCAATCTCTGTTCTGCTCCAGATGCCTTCTAGATTAC  
TGTCTTTTGATTCTTGATTTTCAAGCTTTCAAATCCTCCCTACTTCCAAGAAAATAATTAA  
AAAAAAACTTCATTCTAA

**FIGURE 73**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45493  
><subunit 1 of 1, 518 aa, 1 stop  
><MW: 56180, pI: 5.08, NX(S/T): 2  
MGALARALLLPLLAQWLLRAAPELAPAPFTLPLRVAAATNRVVAPTGP GTPAERHADGLAL  
ALEPALASPAGAAANFLAMVDNLQGD SGRGYYLEMLIGTPPQKLQILVDTGSSNFAVAGTPHS  
YIDTYFDTERSSTYRSKGFDTV KYTQGSWTGFVGEDLVTIPKGFNTSFLVNIATIFESENF  
FLPGIKWNGILGLAYATLAKPSSSLETFFDSLVTQANIPNVFSMQMCGAGLPVAGSGTNGGS  
LVLGGIEPSLYKGDIWYTPIKEEWYYQIEILKLEIGGQSLNLD CREYNADKAIVDSGTTLLR  
LPQKVFD AVEAVARASLIPEFSDGFWTGSQ LACWTNSETPWSYFPKIS IYLRDENS SR SFR  
ITILPQLYIQPMMGAGLNYECYRFGISPSTNALVIGATVMEGFYVIFDRAQKRVGF AASPCA  
EIAGAAVSEISGPFSTEDVASNCVPAQSLSEPILWIVSYALMSVCGAILLV LIVLLLLPFR C  
QRRPRDPEVVNDESSLVRHRWK

**Important features:****Signal peptide:**

amino acids 1-20

**Transmembrane domain:**

amino acids 466-494

**N-glycosylation sites.**

amino acids 170-173 and 366-369

**Leucine zipper pattern.**

amino acids 10-31 and 197-118

**Eukaryotic and viral aspartyl proteases**

amino acids 109-118, 252-261 and 298-310

**FIGURE 74**

CGCCTCCGCCTTCGGAGGCTGACGCGCCCGGGCGCCGTTCCAGGCCTGTGCAGGGCGGATCG  
GCAGCCGCCTGGCGGCGATCCAGGGCGGTGCGGGGCTGGGCGGGAGCCGGGAGGCGCGGCC  
GGCATGGAGGCGCTGCTGCTGGGCGCGGGGTTGCTGCTGGGCGCTTACGTGCTTGTCTACTA  
CAACCTGGTGAAGGCCCCGCCGTGCGGCGGCATGGGCAACCTGCGGGGCCGCACGGCCGTGG  
TCACGGGCGCCAACAGCGGCATCGGAAAGATGACGGCGCTGGAGCTGGCGCGCCGGGAGCG  
CGCGTGGTGGCTGGCCTGCCGCAGCCAGGAGCGCGGGGAGGCGGCTGCCTTCGACCTCCGCCA  
GGAGAGTGGGAACAATGAGGTCATCTTCATGGCCTTGGACTTGGCCAGTCTGGCCTCGGTGC  
GGGCCTTTGCCACTGCCTTTCTGAGCTCTGAGCCACGGTTGGACATCCTCATCCACAATGCC  
GGTATCAGTTCCTGTGGCCGGACCCGTGAGGCGTTTAACCTGCTGCTTCGGGTGAACCATAT  
CGGTCCCTTTCTGCTGACACATCTGCTGCTGCCTTGCTGAAGGCATGTGCCCTAGCCGCG  
TGGTGGTGGTAGCCTCAGCTGCCCCACTGTCGGGGACGTCTTGACTTCAAACGCCTGGACCGC  
CCAGTGGTGGGCTGGCGGCAGGAGCTGCGGGCATATGCTGACACTAAGCTGGCTAATGTACT  
GTTTGGCCGGGAGCTCGCCAACCAGCTTGAGGCCACTGGCGTCACCTGCTATGCAGCCCACC  
CAGGGCCTGTGAACCTCGGAGCTGTTCTGCGCCATGTTCTTGATGGCTGCGCCCACTTTTG  
CGCCCATTTGGCTTGGCTGGTGGTCTCGGGCACCAAGAGGGGGTGCCAGACACCCCTGTATTG  
TGCTCTACAAGAGGGGCATCGAGCCCCCTCAGTGGGAGATATTTTGCCAACTGCCATGTGGAAG  
AGGTGCCTCCAGCTGCCCGAGACGACCGGGCAGCCCATCGGCTATGGGAGGCCAGCAAGAGG  
CTGGCAGGGCTTGGGCCTGGGGAGGATGCTGAACCCGATGAAGACCCCCAGTCTGAGGACTC  
AGAGCCCCCATCTTCTCTAAGCACCCCCCACCCTGAGGAGCCCACAGTTTCTCAACCTTACC  
CCTGCCCTCAGAGCTCAACAGATTTGTCTAAGATGACGCACCGAATTCAGGCTAAAGTTGAG  
CCTGAGATCCAGCTCTCCTAACCCCTCAGGCCAGGATGCTTGCCATGGCACTTCATGGTCCTT  
GAAAACCTCGGATGTGTGTGAGGCCATGCCCTGGACACTGACGGGTTTGTGATCTTGACCTC  
CGTGGTTACTTTCTGGGGCCCCAAGCTGTGCCCTGGACATCTCTTTTCTGGTTGAAGGAAT  
AATGGGTGATTATTTCTTCTGAGAGTGACAGTAACCCAGATGGAGAGATAGGGGTATGCT  
AGACACTGTGCTTCTCGGAAATTTGGATGTAGTATTTTCAGGCCCCACCCTTATTGATTCTG  
ATCAGCTCTGGAGCAGAGGCAGGGAGTTTGCAATGTGATGCACTGCCAACATTGAGAATTAG  
TGAACCTGATCCCTTTGCAACCGTCTAGCTAGGTAGTTAAATTACCCCATGTTAATGAAGCG  
GAATTAGGCTCCCGAGCTAAGGGACTCGCCTAGGGTCTCACAGTGAGTAGGAGGAGGGCCTG  
GGATCTGAACCCAAGGGTCTGAGGCCAGGGCCGACTGCCGTAAGATGGGTGCTGAGAAGTGA  
GTCAGGGCAGGGCAGCTGGTATCGAGGTGCCCCATGGGAGTAAGGGGACGCCTTCCGGGCGG  
ATGCAGGGCTGGGGTCATCTGTATCTGAAGCCCCCTCGGAATAAAGCGCGTTGACCGCCAAAA  
AAAAAAAAAAAAAAAAAA



**FIGURE 75**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48227

<subunit 1 of 1, 377 aa, 1 stop

<MW: 40849, pI: 7.98, NX(S/T): 0

MEALLLGAGLLLGA YVLVYYNLVKAPPCGGMGNLRGRTAVVTGANSIGIGKMTALELARRGAR  
VVLACRSQERGEAAAFDLRQESGNNEVIFMALDLASLASVRAFATAFLSSEPRLDILIHNAG  
ISSCGRTREAFNLLLRVNHIGPFLLTHLLLPCLKACAPSRVVVVASAAHCRGRLDKRLDRP  
VVGWRQELRAYADTKLANVLFARELANQLEATGVTCYAAHPGPVNSELFLRHVPGWLRPLLR  
PLAWLVLRAPRGGGAQTPLYCALQEGIEPLSGRYFANCHVEEVPPAARDRAAHLWEASKRL  
AGLGPGEDAEPDED PQSEDSEAPSSLSTPHPEEPTVSQPYPSPOSSPDLSKMTTHRIQAKVEP  
EIQLS

**Important features:**

**Signal peptide:**

amino acids 1-16

**Glycosaminoglycan attachment site.**

amino acids 46-49

**Short-chain alcohol dehydrogenase family**

amino acids 37-49 and 114-124

**FIGURE 76A**

GGAGGAGACAGCCTCCTGGGGGGCAGGGGTTCCCTGCTCTGCTGCTCCTGCTCATCATGGG  
AGGCATGGCTCAGGACTCCCCGCCCCAGATCCTAGTCCACCCCCAGGACCAGCTGTTCCAGG  
GCCCTGGCCCTGCCAGGATGAGCTGCCAAGCCTCAGGCCAGCCACCTCCCACCATCCGCTGG  
TTGCTGAATGGGCAGCCCCCTGAGCATGGTGGCCCCAGACCCACACCACCTCCTGCTGATGG  
GACCCTTCTGCTGCTACAGCCCCCTGCCCCGGGACATGCCACAGATGGCCAGGCCCCGTCCA  
CAGACCTGGGTGTCTACACATGTGAGGCCAGCAACCGGCTTGGCACGGCAGTCAGCAGAGGC  
GCTCGGCTGTCTGTGGCTGTCTCCGGGAGGATTTCCAGATCCAGCCTCGGGACATGGTGGC  
TGTGGTGGGTGAGCAGTTTACTCTGGAATGTGGGCCGCCCTGGGGCCACCCAGAGCCCACAG  
TCTCATGGTGGAAGATGGGAAACCCCTGGCCCTCCAGCCCGGAAGGCACACAGTGTCCGGG  
GGTCCCTGCTGATGGCAAGAGCAGAGAAGAGTGACGAAGGGACCTACATGTGTGTGGCCAC  
CAACAGCGCAGGACATAGGGAGAGCCGCGCAGCCCCGGGTTTCCATCCAGGAGCCCCAGGACT  
ACACGGAGCCTGTGGAGCTTCTGGCTGTGCGAATTACAGCTGGAAAATGTGACACTGCTGAAC  
CCGGATCCTGCAGAGGGCCCCAAGCCTAGACCGGCGGTGTGGCTCAGCTGGAAGGTCAGTGG  
CCCTGCTGCGCCTGCCAATCTTACACGGCCTTGTTTCCAGGACCCAGACTGCCCCGGGAGGCC  
AGGAGCTCCGTGGGCAGAGGAGCTGCTGGCCGGCTGGCAGAGCGCAGAGCTTGGAGGCCCTC  
CACTGGGGCCAAAGACTACGAGTTCAAAGTGAGACCATCCTCTGGCCGGGCTCGAGGCCCTGA  
CAGCAACGTGCTGCTCTGAGGCTGCCGGAAAAAGTGCCAGTGCCCCACCTCAGGAAGTGA  
CTCTAAAGCCTGGCAATGGCACTGTCTTGTGAGCTGGGTCCCACCACCTGCTGAAAACAC  
AATGGCATCATCCGTGGCTACCAGGTCTGGAGCCTGGGCAACACATCACTGCCACCAGCCAA  
CTGGACTGTAGTTGGTGAGCAGACCCAGCTGGAAATCGCCACCCATATGCCAGGCTCCTACT  
GCGTGCAAGTGGCTGCAGTCACTGGTGTGGAGCTGGGGAGCCAGTAGACCTGTCTGCCTC  
CTTTTAGAGCAGGCCATGGAGCGAGCCACCCAAGAACCAGTGAGCATGGTCCCTGGACCCT  
GGAGCAGCTGAGGGCTACCTTGAAGCGGCTGAGGTCAATTGCCACCTGCGGTGTTGCACTCT  
GGCTGCTGCTTCTGGGCACCGCCGTGTGTATCCACCGCCGGCGCCGAGCTAGGGTGCACCTG  
GGCCAGGTCTGTACAGATATACCAGTGAGGATGCCATCCTAAAACACAGGATGGATCACAG  
TGACTCCCAGTGGTTGGCAGACACTTGGCGTTCCACCTCTGGCTCTCGGGACCTGAGCAGCA  
GCAGCAGCCTCAGCAGTCGGCTGGGGGCGGATGCCCGGGACCCACTAGACTGTGCTCGCTCC  
TTGCTCTCCTGGGACTCCCGAAGCCCCGGCGTGCCCTGCTTCCAGACACCAGCACTTTTTTA  
TGGCTCCCTCATCGCTGAGCTGUCCTCCAGTACCCAGCCAGGCCAAGTCCCCAGGTCCCAG  
CTGTACAGGCGCCTCCCACCCAGCTGGCCAGCTCTCCAGCCCCGTGTTCCAGCTCAGACAGC  
CTCTGCAGCCGCAGGGGACTCTCTTCTCCCCGCTTGCTCTGGCCCCCTGCAGAGGCTTGGAA  
GGCCAAAAGAAGCAGGAGCTGCAGCATGCCAACAGTTCCCCACTGCTCCGGGGCAGCCACT  
CCTTGGAGCTCCGGGCCTGTGAGTTAGGAAATAGAGGTTCCAAGAACCTTTCCCAAAGCCCA  
GGAGCTGTGCCCCAAGCTCTGGTTGCCTGGCGGGCCCTGGGACCGAAACTCCTCAGCTCCTC  
AAATGAGCTGGTTACTCGTCATCTCCCTCCAGCACCCCTCTTTCCTCATGAAACTCCCCAA  
CTCAGAGTCAACAGACCCAGCCTCCGGTGGCACCACAGGCTCCCTCCTCCATCCTGCTGCCA  
GCAGCCCCCATCCCCATCCTTAGCCCCGTGAGTCCCCCTAGCCCCCAGGCCTCTTCCCTCTC  
TGGCCCCAGCCAGCTTCCAGTCGCTGTCCAGCTCCTCACTGTATCCCTGGGGGAGGATC  
AAGACAGCGTGCTGACCCCTGAGGAGGTAGCCCTGTGCTTGGAACTCAGTGAGGGTGAGGAG  
ACTCCCAGGAACAGCGTCTCTCCCATGCCAAGGGCTCCTTACCCCCCACCACCTATGGGTA  
CATCAGCGTCCCAACAGCCTCAGAGTTCACGGACATGGGCAGGACTGGAGGAGGGGTGGGGC  
CCAAGGGGGGAGTCTTGCTGTGCCACCTCGGCCCTGCCTCACCCCCACCCCCAGCGAGGGC  
TCCTTAGCCAATGGTTGGGGCTCAGCCTCTGAGGACAATGCCGCCAGCGCCAGAGCCAGCCT  
TGTCAGCTCCTCCGATGGCTCCTTCTCGCTGATGCTCACTTTGCCCGGGCCCTGGCAGTGG  
CTGTGGATAGCTTTGGTTTTCGGTCTAGAGCCAGGGAGGCAGACTGCGTCTTCATAGATGCC  
TCATCACCTCCCTCCCCACGGGATGAGATCTTCTTGACCCCCAACCTCTCCCTGCCCCCTGTG  
GGAGTGGAGGCCAGACTGGTTGGAAGACATGGAGGTCAGCCACACCCAGCGGTGGGAAGGG  
GGATGCCTCCCTGGCCCCCTGACTCTCAGATCTCTTCCAGAGAAGTCAGCTCCACTGTCTGT  
ATGCCAAAGGCTGGTGCTTCTCCTGTAGATTACTCTGAACCGTGTCCCTGAGACTTCCCAG  
ACGGGAATCAGAACCCTTCTCCTGTCCACCCACAAGACCTGGGCTGTGGTGTGGGTCTT  
GGCCTGTGTTTCTCTGCAGCTGGGGTCCACCTTCCCAAGCCTCCAGAGAGTCTCCCTCCAC  
GATTGTGAAAACAAATGAAAACAAATTAGAGCAAAGCTGACCTGGAGCCCTCAGGGAGCAA  
AACATCATCTCCACCTGACTCCTAGCCACTGCTTTCTCCTCTGTGCCATCCACTCCCACCAC  
CAGGTTGTTTTGGCCTGAGGAGCAGCCCTGCCTGCTGCTCTTCCCCCACCATTGGATCACA

**FIGURE 76B**

GGAAGTGGAGGAGCCAGAGGTGCCTTTGTGGAGGACAGCAGTGGCTGCTGGGAGAGGGCTGT  
GGAGGAAGGAGCTTCTCGGAGCCCCCTCTCAGCCTTACCTGGGCCCCCTCCTCTAGAGAAGAG  
CTCAACTCTCTCCCAACCTCACCATGGAAAGAAAATAATTATGAATGCCACTGAGGCACTGA  
GGCCCTACCTCATGCCAAACAAAGGGTTCAAGGCTGGGTCTAGCGAGGATGCTGAAGGAAGG  
GAGGTATGAGACCGTAGGTCAAAAGCACCATCCTCGTACTGTTGTCACTATGAGCTTAAGAA  
ATTTGATACCATAAAATGGTAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

**FIGURE 77**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA41404  
<subunit 1 of 1, 985 aa, 1 stop  
<MW: 105336, pI: 6.55, NX(S/T): 7  
MGGMAQDSPPQILVHPQDQLFQGPGRMSCQASGQPPPTIRWLLNGQPLSMVPPDPHLLP  
DGTLLLLQPPARGHAHDGQALSTD LGVYTCEASNRLGTAVSRGARLSVAVLREDFQIQPRDM  
VAVVGEQFTLECGPPWGHPEPTVSWWKDGKPLALQPRHTVSGGSLLMARA EKSDEGT YMCV  
ATNSAGHRESRAARVSIQEPQDYTEPV ELLAVRIQLENTLLNPDPAEGPKPRPAVWLSWKV  
SGPAAPAQSYTALFRTQTAPGGQGAPWAEELLAGWQSAELGGLHWGQDYEFKVRPSSGRARG  
PDSNVLLLLRLPEKVPSAPPQEVTLKPGNGTVFVSWVPPPAENHNGIIRGYQVWSLGNTSLPP  
ANWTVVGEQTOLEIATHMPGSYCVQVA AVTGAGAGEPSRPVCLLLEQAMERATQEPSEHG PW  
TLEQLRATLKRPEVIATCGVALWLLLLGTAVCIHRRRRARVHLGPGLYRYTSEDAILKHRMD  
HSDSQWLADTWRSTSGSRDLSSSSSLSSRLGADARDPLDCRRSLLSWDSRSPGVPLLPDTST  
FYGSLIAELPSSTPARPSPQVPAVRRLPPQLAQLSSPCSSSDSLCSRRGLSSPRLSLAPAEA  
WKAKKKQELQHANS SPLL RGS HSLELRACELGNRGSKNLSQSPGAVPQALVAWRALGPKLLS  
SSNELVTRHLPAPLFP HETPPTQSQQTQPPVAPQAPSSILLPAAPIPILSPCSPPSPQASS  
LSGPSPASSRLSSSSSLSLGEDQDSVLTPEEVALCLELSEGEETPRNSVSPMPRAPSPPTTY  
GYISVPTASEFTDMGRTGGGVGPKGGVLLCPPRPCLTPTPSEGLANGWSASEDNAASARA  
SLVSSSDGSFLADAHFARALAVAVDSFGFGLPREADCVFIDASSPPSPRDEIFLTPNLSLP  
LWEWRPDWLEDMEVSHTQRLGRGMPPWPPDSQISSQRSQLHCRMPKAGASPV DYS

**Important features:**

**Transmembrane domain:**

amino acids 448-467

**N-glycosylation sites:**

amino acids 224-227, 336-341, 367-370, 374-377, 658-661 and 926-929

**N-myristoylation sites.**

amino acids 47-52, 80-85, 88-93, 99-104, 105-110, 181-186, 272-277, 290-295, 355-360, 403-408, 462-467, 561-566, 652-657, 849-854 and 876-881

**Phosphotyrosine interaction domain proteins**

amino acids 740-753

**FIGURE 78**

CTCCACGGTGTCCAGCGCCAGAAATGCGGCTTCTGGTCCTGCTATGGGGTTGCCTGCTGCT  
CCCAGGTTATGAAGCCCTGGAGGGCCAGAGGAAATCAGCGGGTTTGAAGGGGACACTGTGT  
CCCTGCAGTGCACCTACAGGGAAGAGCTGAGGGACCACCGGAAGTACTGGTGCAGGAAGGGT  
GGGATCCTCTTCTCTCGCTGCTCTGGCACCATCTATGCAGAAGAAGAAGGCCAGGAGACAAT  
GAAGGGCAGGGTGTCCATCCGTGACAGCCGCCAGGAGCTCTCGCTCATTGTGACCCTGTGGA  
ACCTCACCCCTGCAAGACGCTGGGGAGTACTGGTGTGGGGTCGAAAAACGGGGCCCCGATGAG  
TCTTTACTGATCTCTCTGTTCGTCTTTCCAGGACCCTGCTGTCCTCCCTCCCTTCTCCCAC  
CTTCCAGCCTCTGGCTACAACACGCCTGCAGCCCAAGGCAAAAGCTCAGCAAACCCAGCCCC  
CAGGATTGACTTCTCCTGGGCTCTACCCGGCAGCCACCACAGCCAAGCAGGGGAAGACAGGG  
GCTGAGGCCCCCTCCATTGCCAGGGACTTCCAGTACGGGCACGAAAGGACTTCTCAGTACAC  
AGGAACCTCTCCTCACCCAGCGACCTCTCCTCCTGCAGGGAGCTCCCGCCCCCCCATGCAGC  
TGGACTCCACCTCAGCAGAGGACACCAGTCCAGCTCTCAGCAGTGGCAGCTCTAAGCCCAGG  
GTGTCCATCCCGATGGTCCGCATACTGGCCCCAGTCTGGTGTGCTGAGCCTTCTGTCAGC  
CGCAGGCCTGATCGCCTTCTGCAGCCACCTGCTCCTGTGGAGAAAGGAAGCTCAACAGGCCA  
CGGAGACACAGAGGAACGAGAAGTTCTGGCTCTCACGCTTGACTGCGGAGGAAAAGGAAGCC  
CCTTCCCAGGCCCCCTGAGGGGGACGTGATCTCGATGCCTCCCTCCACACATCTGAGGAGGA  
GCTGGGCTTCTCGAAGTTTGTCTCAGCGTAGGGCAGGAGGCCCTCCTGGCCAGGCCAGCAGT  
GAAGCAGTATGGCTGGCTGGATCAGCACCGATTCCCGAAAGCTTTCACCTCAGCCTCAGAG  
TCCAGCTGCCCGGACTCCAGGGCTCTCCCCACCTCCCGAGGCTCTCCTCTTGATGTTCCA  
GCCTGACCTAGAAGCGTTTGTACGCCCTGGAGCCAGAGCGGTGGCCTTGCTCTTCCGGCTG  
GAGACTGGGACATCCCTGATAGGTTACATCCCTGGGCAGAGTACCAGGCTGCTGACCCTCA  
GCAGGGCCAGACAAGGCTCAGTGGATCTGGTCTGAGTTTCAATCTGCCAGGAACCTCTGGGC  
CTCATGCCCAGTGTGCGGACCCTGCCTTCTCCCACTCCAGACCCACCTTGTCTTCCCTCCC  
TGGCGTCTCAGACTTAGTCCCACGGTCTCCTGCATCAGCTGGTGATGAAGAGGAGCATGCT  
GGGGTGAGACTGGGATTCTGGCTTCTCTTTGAACCACCTGCATCCAGCCCTTCAGGAAGCCT  
GTGAAAAACGTGATTCTGGCCCCACCAAGACCACCAAAACCATCTCTGGGCTTGGTGCAG  
GACTCTGAATTCTAACAATGCCCAGTGACTGTCCGCACTTGAGTTTGAGGGCCAGTGGGCCTG  
ATGAACGCTCACACCCCTTCAGCTTAGAGTCTGCATTTGGGCTGTGACGTCTCCACCTGCCC  
CAATAGATCTGCTCTGTCTGCGACACCAGATCCACGTGGGGACTCCCTGAGSCCTGCTAAG  
TCCAGGCCTTGGTCAGGTCAGGTGCACATTGCAGGATAAGCCCAGGACCGGCACAGAAGTGG  
TTGCCCTTNNCCATTTGCCCTCCCTGGNCCATGCCTTCTTGCTTTGGAAAAAATGATGAAGA  
AAACCTTGGCTCCTTCTTGTCTGGAAAGGGTTACTTGCCTATGGGTTCTGGTGGCTAGAGA  
GAAAAGTAGAAAACCAGAGTGCACGTAGGTGTCTAACACAGAGGAGTAGGAACAGGGCGG  
ATACCTGAAGGTGACTCCGAGTCCAGCCCCCTGGAGAAGGGGTGCGGGGTGGTGGTAAAGTA  
GCACAACTACTATTTTTTTTCTTTTTCCATTATTATTGTTTTTTAAGACAGAATCTCGTGCT  
GCTGCCCAGGCTGGAGTGCAGTGGCAGATCTGCAAACTCCGCCTCCTGGGTTCAAGTGATT  
CTTCTGCCTCAGCCTCCCGAGTAGCTGGGATTACAGGCACGCACCACCACACCTGGCTAATT  
TTTGTACTTTTAGTAGAGATGGGGTTTACCATGTTGGCCAGGCTGGTCTTGAACCTCTGAC  
CTCAAATGAGCCTCCTGCTTCAGTCTCCCAAATTGCCGGGATTACAGGCATGAGCCACTGTG  
TCTGGCCCTATTTCTTTAAAAAGTGAAATTAAGAGTTGTTCAGTATGCAAACTTGGAAG  
ATGGAGGAGAAAAAGAAAAGGAAGAAAAAATGTCACCCATAGTCTCACCAGAGACTATCAT  
TATTTTCGTTTTGTGTACTTCCTTCCACTCTTTTCTTCTTACATAATTTGCCGGTGTCTT  
TTTACAGAGCAATTATCTTGTATATACACTTTGTATCCTGCCTTTTCCACCTTATCGTTCC  
ATCACTTTATTCCAGCACTTCTGTGTTTTACAGACCTTTTTTATAAATAAAATGTTTCATCA  
GCTGCATAAAAAAAAAAAAAA

**FIGURE 79**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44196

<subunit 1 of 1, 332 aa, 1 stop

<MW: 36143, pI: 5.89, NX(S/T): 1

MRLLVLLWGCLLLPGYEALLEGPEEISGFEGDTVSLQCTYREELRDHRKYWCRKGGILFSRCS  
GTIYAE EEGQETMKGRVSIRDSRQELSLIVTLWNLTLDAGEYWCGVEKRGPD E SLLISLFV  
FPGPCCPPSPSPPTFQPLATTRLQPKAKAQQTQPPGLTSPGLYPAATTAKQKTGA EAPPLPG  
TSQYGHERTSQYTGTSPHPATSPAGSSRPPMQLDSTSAEDTSPALSSGSSKPRVSIPMVRI  
LAPVLVLLSLLSAAGLIAFCSHLLLWRKEAQQATETQRNEKFWLSRLTAE EKEAPSQAPEGD  
VISMPPLHTSEEEELGFSKFVSA

**Important features:**

**Signal peptide:**

amino acids 1-17

**Transmembrane domain:**

amino acids 248-269

**N-glycosylation site.**

amino acids 96-99

**Fibrinogen beta and gamma chains C-terminal domain.**

amino acids 104-113

**Ig like V-type domain:**

amino acids 13-128

**FIGURE 80**

TTGTGACTAAAAGCTGGCCTAGCAGGCCAGGGAGTGCAGCTGCAGGCGTGGGGGTGGCAGGA  
GCCGCAGAGCCAGAGCAGACAGCCGAGAAACAGGTGGACAGTGTGAAAGAACCAGTGGTCTC  
GCTCTGTTGCCCAGGCTAGAGTGTACTGGCGTGATCATAGCTCACTGCAGCCTCAGACTCCT  
GGACTTGAGAAATCCTCCTGCCTTAGCCTCCTGCATATCTGGGACTCCAGGGGTGCACTCAA  
GCCCTGTTTCTTCTCCTTCTGTGAGTGGACCACGGAGGCTGGTGAGCTGCCTGTATCCCAA  
AGCTCAGCTCTGAGCCAGAGTGGTGGTGGCTCCACCTCTGCCGCCGGCATAGAAGCCAGGAG  
CAGGGCTCTCAGAAGGCGGTGGTGCCAGCTGGGATCATGTTGTTGGCCCTGGTCTGTCTGC  
TCAGCTGCCTGCTACCCTCCAGTGAGGCCAAGCTCTACGGTCGTTGTGAACTGGCCAGAGTG  
CTACATGACTTCGGGCTGGACGGATACCGGGGATACAGCCTGGCTGACTGGGTCTGCCTTGC  
TTATTTACAAGCGGTTTCAACGCAGCTGCTTTGGACTACGAGGCTGATGGGAGCACCAACA  
ACGGGATCTTCCAGATCAACAGCCGGAGGTGGTGCAGCAACCTCACCCCGAACGTCCCCAAC  
GTGTGCCGGATGTACTGCTCAGATTTGTTGAATCCTAATCTCAAGGATACCGTTATCTGTGC  
CATGAAGATAACCCAAGAGCCTCAGGGTCTGGGTTACTGGGAGGCCTGGAGGCATCACTGCC  
AGGGAAAAGACCTCACTGAATGGGTGGATGGCTGTGACTTCTAGGATGGACGGAACCATGCA  
CAGCAGGCTGGGAAATGTGGTTTGGTTCCTGACCTAGGCTTGGAAGACAAGCCAGCGAATA  
AAGGATGGTTGAACGTGAAA

**FIGURE 81**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA52187

<subunit 1 of 1, 146 aa, 1 stop

<MW: 16430, pI: 5.05, NX(S/T): 1

MLLALVCLLSCLLPSSSEAKLYGRCELARVLHDFGLDGYRGYSLADWVCLAYFTSGFNAAALD  
YEADGSTNNGIFQINSRRWCSNLTPNVPNVCRMYSDDLNPNLKDTVICAMKITQEPQGLGY  
WEAWRHHCQGKDLTEWVDGPDF

**Important features:**

**Signal peptide:**

amino acids 1-18

**N-myristoylation site.**

amino acids 67-72

**Homologous region to Alpha-lactalbumin / lysozyme C proteins.**

amino acids 34-58 (catalytic domain), 111-132 and 66-107



**FIGURE 82**

AGCCGCTGCCCCGGGCGGGCGCCGCGGGCACCATGAGTCCCCGCTCGTGCCTGCGTTC  
GCTGCGCCTCCTCGTCTTCGCCGTCTTCTCAGCCGCCGCGAGCAACTGGCTGTACCTGGCCA  
AGCTGTGCTCGGTGGGGAGCATCTCAGAGGAGGAGACGTGCGAGAACTCAAGGGCCTGATC  
CAGAGGCAGGTGCAGATGTGCAAGCGGAACCTGGAAAGTCATGGACTCGGTGCGCCGCGGTGC  
CCAGCTGGCCATTGAGGAGTGCCAGTACCAGTTCCGGAACCGGCGCTGGAAGTCTCCACAC  
TCGACTCCTTGCCCGTCTTCGGCAAGGTGGTGACGCAAGGGACTCGGGAGGCGGCCTTCGTG  
TACGCCATCTCTTCGGCAGGTGTGGCCTTTGCAGTGACGCGGGCGTGCAGCAGTGGGGAGCT  
GGAGAAGTGCGGCTGTGACAGGACAGTGCATGGGGTCAGCCACAGGGCTTCCAGTGGTCAG  
GATGCTCTGACAACATCGCCTACGGTGTGGCCTTCTCACAGTCGTTTGTGGATGTGCGGGAG  
AGAAGCAAGGGGGCCTCGTCCAGCAGAGCCCTCATGAACCTCCACAACAATGAGGCCGGCAG  
GAAGGCCATCCTGACACACATGCGGGTGGAAATGCAAGTGCCACGGGGTGTGAGGCTCCTGTG  
AGGTAAAGACGTGCTGGCGAGCCGTGCCGCCCTTCCGCCAGGTGGGTACGCACTGAAGGAG  
AAGTTTGATGGTGCCACTGAGGTGGAGCCACGCCCGTGGGCTCCTCCAGGGCACTGGTACC  
ACGCAACGCACAGTTCAAGCCGCACACAGATGAGGACCTGGTGTACTTGGAGCCTAGCCCCG  
ACTTCTGTGAGCAGGACATGCGCAGCGGCGTGCTGGGCACGAGGGGCCGCACATGCAACAAG  
ACGTCCAAGGCCATCGACGGCTGTGAGCTGCTGTGCTGTGGCCGCGGCTTCCACACGGCGCA  
GGTGGAGCTGGCTGAACGCTGCAGCTGCAAATTCCTGCTGCTTTCGTCAAGTGCCGGC  
AGTGCCAGCGGCTCGTGGAGTTGCACACGTGCCGATGACCGCCTGCCTAGCCCTGCGCCGGC  
AACCACCTAGTGGCCCAGGGAAGGCCGATAATTTAAACAGTCTCCCACCACCTACCCCAAGA  
GATACTGGTTGTATTTTTTGTCTCGTTTGGTTTTTGGGTCCTCATGTTATTTATTGCCGAA  
ACCAGGCAGGCAACCCCAAGGGCACCAACCAGGGCCTCCCCAAAGCCTGGGCCTTTGTGGCT  
GCCACTGACCAAAGGGACCTTGCTCGTGCCGCTGGCTGCCCGCATGTGGCTGCCACTGACCA  
CTCAGTTGTTATCTGTGTCCGTTTTTCTACTTGACAGACCTAAGGTGGAGTAACAAGGAGTAT  
TACCACCACATGGCTACTGACCGTGTGTCATCGGGGAAGAGGGGGCCTTATGGCAGGGAAAATA  
GGTACCGACTTGATGGAAGTCACACCCTCTGGAAAAAGAACTCTTAACCTCTCCAGCACACA  
TACACATGGACTCCTGGCAGCTTGAGCCTAGAAGCCATGTCTCTCAAATGCCCTGAGAAAGG  
GAACAAGCAGATACCAGGTCAAGGGCACCAGGTTCAATTCAGCCCTTACATGGACAGCTAGA  
GGTTCGATATCTGTGGGTCTTCCAGGCAAGAAGAGGGAGATGAGAGCAAGAGACGACTGAA  
GTCCCAACCCTAGAACCCAGCCTGCCCCAGCCTGCCCCTGGGAAGAGGAACTTAACCACTCC  
CCAGACCCACCTAGGCAGGCATATAGGCTGCCATCCTGGACCAGGGATCCCGGCTGTGCCTT  
TGCAGTCATGCCCCAGTACCTTTTACAGCGCTGTTCCCTCATGAAACTGAAAAACACACAC  
ACCTGCGAGA  
GAGAGGGAGGAAAGGGCTGTGCCTTTGCAGTCATGCCCGAGTCACCTTTTACAGCACTGTTCTC

**FIGURE 83**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48328

<subunit 1 of 1, 351 aa, 1 stop

<MW: 39052, pI: 8.97, NX(S/T): 2

MSPRSCLRLRLLVFAVFSAAASNWLYLAKLSSVGSISEEETCEKLKGLIQRVQMCKRNLE  
VMDSVRRGAQLAIEECQYQFRNRRWNCSTLDSL PVFGKVVTQGTREAAFVYAISSAGVAFV  
TRACSSGELEKCGCDRTVHGVSPQGFQWSGCS DNIAYGVAFSQS FVDVRERSKGASSSRALM  
NLHNNEAGRKAILTHMRVECKCHGVSGSCEVKT CWRVPPFRQVGHALKEKFDGATEVEPRR  
VGSSRALVPRNAQFKPHTDEDLVYLEPSPDFCEQDMRSGVLGTRGRTC NKTSKAIDGCELLC  
CGRGFHTAQVELAERCSCKFHWCCFVKCRQCQRLVELHTCR

**Important features:**

**Signal peptide:**

amino acids 1-22

**N-glycosylation sites.**

amino acids 88-91 and 297-300

**Wnt-1 family signature.**

amino acids 206-215

**Homologous region to Wnt-1 family proteins**

amino acids 183-235, 305-350, 97-138, 53-92 and 150 -174

**FIGURE 84**

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCTGGGTGCCTGCAT  
CGCCATGGACACCACCAGGTACAGCAAGTGGGGCGGCAGCTCCGAGGAGGTCCCCGGAGGGC  
CCTGGGGACGCTGGGTGCACTGGAGCAGGAGACCCCTCTTCTTGGCCCTGGCTGTCCTGGTC  
ACCACAGTCCTTTGGGCTGTGATTCTGAGTATCCTATTGTCCAAGGCCTCCACGGAGCGCGC  
GGCGCTGCTTGACGGCCACGACCTGCTGAGGACAAACGCCTCGAAGCAGACGGCGGGCGCTGG  
GTGCCCTGAAGGAGGAGGTCTGGAGACTGCCACAGCTGCTGCTCGGGGACGCAGGCGCAGCTG  
CAGACCACGCGCGCGGAGCTTGGGGAGGCGCAGGCGAAGCTGATGGAGCAGGAGAGCGCCCT  
GCGGGAACCTGCGTGAGCGCGTGACCCAGGGCTTGGCTGAAGCCGGCAGGGGCCGTGAGGACG  
TCCGCACTGAGCTGTTCCGGGCGCTGGAGGCCGTGAGGCTCCAGAACAACCTCTGCGAGCCG  
TGCCCCACGTCGTGGCTGTCCTTCGAGGGCTCCTGCTACTTTTTCTCTGTGCCAAAGACGAC  
GTGGGCGGGCGGCGCAGGATCACTGCGCAGATGCCAGCGCGCACCTGGTGATCGTTGGGGGCC  
TGGATGAGCAGGGCTTCCTCACTCGGAACACGCGTGGCCGTGGTTACTGGCTGGGCCTGAGG  
GCTGTGCGCCATCTGGGCAAGGTTTACGGGCTACCAAGTGGGTGGACGGAGTCTCTCTCAGCTT  
CAGCCACTGGAACCAGGGAGAGCCCAATGACGCTTGGGGGCGCGAGAAGTGTGTTCATGATGC  
TGCACACGGGGCTGTGGAACGACGCACCGTGTGACAGCGAGAAGGACGGCTGGATCTGTGAG  
AAAAGGCACAACCTGCTGACCCCGCCAGTGGCCCTGGAGCCGCGCCCATTCGAGCATGTCGTA  
TCCTGGGGGCTGCTCACCTCCCTGGCTCCTGGAGCTGATTGCCAAAGAGTTTTTTCTTCTCT  
CATCCACCGCTGCTGAGTCTCAGAAACACTTGGCCCAACATAGCCCTGTCCAGCCCAGTGCC  
TGGGCTCTGCGACCTCCATGCCGACCTCATCCTAACTCCACTCACGCAGACCCAAACCTAACC  
TCCACTAGCTCCAAAATCCCTGCTCCTGCGTCCCCGTGATATGCTCCACTTCTCTCCCTAA  
CCAAGGTTAGGTGACTGAGGACTGGAGCTGTTTGGTTTTCTCGCATTTTCCACCAAACCTGGA  
AGCTGTTTTTGCAGCCTGAGGAAGCATCAATAAATATTTGAGAAATGAAAAA

**FIGURE 85**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56352

<subunit 1 of 1, 293 aa, 1 stop

<MW: 32562, pI: 6.53, NX(S/T): 2

MDTTRYSKWGSSEEVPGGPWGRVHWSRRPLFLALAVLVTTVLWAVILSILLSKASTERAA  
LLDGHDLRLRTNASKQTAALGALKEEVGDCHSCCSGTQAQLQTTTAEELGEAQAKLMEQESALR  
ELRERVTOGLAEAGRGREDVRTELFRALEAVRLQNNSCPCPTSWLSFEGSCYFFSVPKTTW  
AAAQDHCADASAHLVIVGGLDEQGFLTRNTRGRGYWLGLRAVRHLGKVQGYQWVDGVSLSFS  
HWNQGEPNDAWGRENCVMMMLHTGLWNDAPCDSEKDGWICEKRHNC

**Important features:**

**Type II transmembrane domain:**

amino acids 31-54

**N-glycosylation sites.**

amino acids 73-76 and 159-162

**Leucine zipper pattern.**

amino acids 102-123

**N-myristoylation sites.**

amino acids 18-23, 133-138 and 242-247

**C-type lectin domain signature.**

amino acids 264-287

**FIGURE 86**

GCCAGGGGAAGAGGGTGATCCGACCCGGGAAGGTCGCTGGGCAGGGCGAGTTGGGAAAGCG  
GCAGCCCCCGCCGCCCGCCGAGCCCCCTTCTCCTCCTTTCTCCACGTCCTATCTGCCTCTCG  
CTGGAGGCCAGGCCGTGCAGCATCGAAGACAGGAGGAACTGGAGCCTCATTGGCCGGCCCGG  
GGCGCCGGCCTCGGGCTTAAATAGGAGCTCCGGGCTCTGGCTGGGACCCGACCGCTGCCGGC  
CGCGCTCCCGCTGCTCCTGCCGGGTGATGGAAACCCCGAGCCCGGCCGCCCGCCCTGGGCAAG  
GCCCTCTGCGCTCTCCTCCTGGCCACTCTCGGCGCCGCCGGCCAGCCTCTTGGGGGAGAGTC  
CATCTGTTCCGCCAGAGCCCCGGCCAAATACAGCATCACCTTCACGGGCAAGTGGAGCCAGA  
CGGCCTTCCCCAAGCAGTACCCCCTGTTCCGCCCCCTGCGCAGTGGTCTTCGCTGCTGGGG  
GCCGCGCATAGCTCCGACTACAGCATGTGGAGGAAGAACCAGTACGTCAGTAACGGGCTGCG  
CGACTTTGCGGAGCGCGGCGAGGCCTGGGCGCTGATGAAGGAGATCGAGGCGGCGGGGGAGG  
CGCTGCAGAGCGTGCACGAGGTGTTTTCGGCGCCCGCCGTCCCCAGCGGCACCGGGCAGACG  
TCGGCGGAGCTGGAGGTGCAGCGCAGGCACTCGCTGGTCTCGTTTGTGGTGCGCATCGTGCC  
CAGCCCCGACTGGTTTCGTGGGCGTGGACAGCCTGGACCTGTGCGACGGGGACCGTTGGCGGG  
AACAGGCGGGCGCTGGACCTGTACCCCTACGACGCCGGGACGGACAGCGGCTTCACCTTCTCC  
TCCCCCAACTTCGCCACCATCCCGCAGGACACGGTGACCGAGATAACGTCCTCCTCTCCAG  
CCACCCGGCCAACCTCTTCTACTACCCGCGGCTGAAGGCCCTGCCTCCCATCGCCAGGGTGA  
CACTGCTGCGGCTGCGACAGAGCCCCAGGGCCTTCATCCCTCCCGCCCCAGTCTGCCCAGC  
AGGGACAATGAGATTGTAGACAGCGCTCAGTTCCAGAAACGCCGCTGGACTGCGAGGTCTC  
CCTGTGGTTCGTCTGGGGACTGTGCGGAGGCCACTGTGGGAGGCTCGGGACCAAGAGCAGGA  
CTCGCTAGGTCCGGGTCCAGCCCGCCAACAACGGGAGCCCTGCCCGAGCTCGAAGAAGAG  
GCTGAGTGCGTCCCTGATAACTGCGTCTAAGACCAGAGCCCCGAGCCCTGGGGCCCCCGG  
GAGCCATGGGGTGTCGGGGGCTCCTGTGCAGGCTCATGCTGCAGGCGGCCGAGGGCACAGGG  
GGTTTCGCGCTGCTCCTGACCGCGGTGAGGCCGCGCCGACCATCTCTGCACTGAAGGGCCCT  
CTGGTGGCCGGCACGGGCATTGGGAAACAGCCTCCTCCTTTCCCAACCTTGCTTCTTAGGGG  
CCCCCGTGTCCCGTCTGCTCTCAGCCTCCTCCTCCTGCAGGATAAAGTCATCCCCAAGGCTC  
CAGCTACTCTAAATTATGTCTCCTTATAAGTTATTGCTGCTCCAGGAGATTGTCCTTCATCG  
TCCAGGGGCCTGGCTCCCACGTGGTTGCAGATACCTCAGACCTGGTGCTCTAGGCTGTGCTG  
AGCCCACTCTCCCGAGGGCGCATCCAAGCGGGGGCCACTTGAGAAGTGAATAAATGGGGCGG  
TTTCGGAAGCGTCAGTGTTTCCATGTTATGGATCTCTCTGCGTTTGAATAAAGACTATCTCT  
GTTGCTCACAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

**FIGURE 87**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA53971

><subunit 1 of 1, 331 aa, 1 stop

><MW: 35844, pI: 5.45, NX(S/T): 2

MENPSPAAALGKALCALLLATLGAAGQPLGGESICSARAPAKYSITFTGKWSQTAFPKQYPL  
FRPPAQWSSLLGAAHSSDYSMWRKNQYVSNGLRDFEAERGEAWALMKEIEAAGEALQSVHEVF  
SAPAVPSGTGQTSAELEVQRRHSLVSFVVRIVPSPDWFGVDSLDLCDGDRWREQAALDLYP  
YDAGTDSGFTFSSPNFATIPQDTVTEITSSSPSHPANSFYYPRLKALPPIARVTLLRLRQSP  
RAFIPPAPVLP SRDNEIVDSASVPETPLDCEVSLWSSWGLCGGHCGR LGTKSRTRYVRVQPA  
NNGSPCPELEEEAECPDNCV

**Important features:**

**Signal peptide:**

amino acids 1-26

**FIGURE 88**

GGCGGCGTCCGTGAGGGGCTCCTTTGGGCAGGGGTAGTGTTTGGTGTCCCTGTCTTGCGTGA  
TATTGACAAACTGAAGCTTTCCTGCACCACTGGACTTAAGGAAGAGTGTACTCGTAGGCGGA  
CAGCTTTAGTGGCCGGCCGGCCGCTCTCATCCCCGTAAGGAGCAGAGTCCTTTGTACTGAC  
CAAGATGAGCAACATCTACATCCAGGAGCCTCCCACGAATGGGAAGGTTTTATTGAAAACATA  
CAGCTGGAGATATTGACATAGAGTTGTGGTCCAAAGAAGCTCCTAAAGCTTGCAGAAATTTT  
ATCCAACCTTTGTTTGAAGCTTATTATGACAATACCATTTTTTCATAGAGTTGTGCCTGGTTT  
CATAGTCCAAGGCGGAGATCCTACTGGCACAGGGAGTGGTGGAGAGTCTATCTATGGAGCGC  
CATTCAAAGATGAATTTCAATCACGGTTGCGTTTTAATCGGAGAGGACTGGTTGCCATGGCA  
AATGCTGGTTCTCATGATAATGGCAGCCAGTTTTTCTTCACACTGGGTCGAGCAGATGAACT  
TAACAATAAGCATAACCATCTTTGGAAAGGTTACAGGGGATACAGTATATAACATGTTGCGAC  
TGTCAGAAGTAGACATTGATGATGACGAAAGACCACATAATCCACACAAAATAAAAAGCTGT  
GAGGTTTTGTTTAATCCTTTTGATGACATCATTCCAAGGGAAATTAAAAGGCTGAAAAAGA  
GAAACCAGAGGAGGAAGTAAAGAAATTGAAACCCAAAGGCACAAAAAATTTTAGTTTACTTT  
CATTTGGAGAGGAAGCTGAGGAAGAAGAGGAGGAAGTAAATCGAGTTAGTCAGAGCATGAAG  
GGCAAAGCAAAGTAGTCATGACTTGCTTAAGGATGATCCACATCTCAGTTCTGTTCAGT  
TGTAAGAAAGTAAAAAGGTGATGCACCAGATTTAGTTGATGATGGAGAAGATGAAAGTGCAG  
AGCATGATGAATATATTGATGGTGATGAAAAGAACCTGATGAGAGAAAGAATTGCCAAAAAA  
TTAAAAAAGGACACAAGTGCGAATGTTAAATCAGCTGGAGAAGGAGAAGTGGAGAAGAAATC  
AGTCAGCCGCACTGAAGAGCTCAGAAAAGAAGCAAGACAATTAAAACGGGAACCTCTTAGCAG  
CAAAACAAAAAAGTAGAAAATGCAGCAAAACAAGCAGAAAAAAGAAGTGAAGAGGAAGAA  
GCCCCCTCCAGATGGTGCTGTTGCCGAATACAGAAGAGAAAAGCAAAGTATGAAGCTTTGAG  
GAAGCAACAGTCAAAGAAGGGAACCTCCCGGGAAGATCAGACCCTTGCACTGCTGAACCAGT  
TTAAATCTAAACTCACTCAAGCAATTGCTGAAACACCTGAAAATGACATTCCTGAAACAGAA  
GTAGAAGATGATGAAGGATGGATGTCACATGTACTTCAGTTTGAGGATAAAAGCAGAAAAGT  
GAAAGATGCAAGCATGCAAGACTCAGATACATTTGAAATCTATGATCCTCGGAATCCAGTGA  
ATAAAAGAAGGAGGGAAGAAAGCAAAGCTGATGAGAGAGAAAAAGAAAGAAGATAAAAT  
GAGAATAATGATAACCAGAACTTGCTGGAAATGTGCCTACAATGGCCTTGTAACAGCCATTG  
TTCCCAACAGCATCACTTAGGGGTGTGAAAAGAAGTATTTTGAACCTGTTGTCTGGTTTTG  
AAAAACAATTATCTTGTGTTTGCAAATTGTGGAATGATGTAAGCAAATGCTTTTGGTTACTGG  
TACATGTGTTTTTTTCCTAGCTGACCTTTTATATTGCTAAATCTGAAATAAAATAACTTTCCT  
TCCACAAAAA

90/237

**FIGURE 89**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50919  
><subunit 1 of 1, 472 aa, 1 stop  
><MW: 53847, pI: 5.75, NX(S/T): 2  
MSNIYIQEPPTNGKVLLKTTAGDIDIELWSKEAPKACRNFIQLCLEAYYDNTIFHRVVPGFI  
VQGGDPTGTGSGGESIYGAPFKDEFHSRLRFNRRGLVAMANAGSHDNGSQFFFTLGRADELN  
NKHTIFGKVTGDTVYNMLRLSEVDIDDDERPHNPHKIKSCEVLNPFDDIIPREIKRLKKEK  
PEEEVKKLKPKGTKNFSLLSFGEAAEEEEEEVNRVSQSMKGKSKSSHDLKDDPHLSSVPVW  
ESEKGDAPDLVDDGEDESAEHDEYIDGDEKNLMRERIAKKLKKDTSANVKSAGEGEVEKKSV  
SRSEELRKEARQLKRELLAAKQKKVENAAKQAEKRSEEEEAPPDGAVAEYRREKQKYEALRK  
QQSKKGTSREDQTLALLNQFKSKLTQAIATPENDIPETEVEDDEGWMSHVLQFEDKSRKVK  
DASMQDSDTFEIIYDPRNPVKNRRREESKKLMREKKERR

**Important features:****Signal peptide:**

amino acids 1-21

**N-glycosylation sites.**

amino acids 109-112 and 201-204

**Cyclophilin-type peptidyl-prolyl cis-trans isomerase signature.**

amino acids 49-66

**Homologous region to Cyclophilin-type peptidyl-prolyl cis-trans isomerase**

amino acids 96-140, 49-89 and 22-51



**FIGURE 90**

CGCCGCCGTTGGGGCTGGAAGTTCCCGCCAGGTCCGTGCCGGGCGAGAGAGATGCTGCCCGG  
CCCGCCTCGGCTTTGAGGCGAGAGAAGTGTCCAGACCCATTTGCGCTTGCTGACGGCGTCG  
AGCCCTGGCCAGACATGTCCACAGGGTTCTCCTTCGGGTCCGGGACTCTGGGCTCCACCACC  
GTGGCCGCCGGCGGGACCAGCACAGGCGGCGTTTTCTCCTTCGGAACGGGAACGTCTAGCAA  
CCCTTCTGTGGGGCTCAATTTTGGAATCTTGGAAGTACTTCAACTCCAGCAACTACATCTG  
CTCCTTCAAGTGGTTTTTGGAACCGGGCTCTTTGGATCTAAACCTGCCACTGGGTTCACTCTA  
GGAGGAACAAATACAGGTGCCTTGACACCAAGAGGCCCTCAAGTGGTCACCAATATGGAAC  
CCTGCAAGGAAAACAGATGCATGTGGGGAAGACACCCATCCAAGTCTTTTAGGAGTCCCTT  
TCTCCAGACCTCCTCTAGGTATCCTCAGGTTTGACCTCCAGAACCCCCGGAGCCCTGGAAA  
GGAATCAGAGATGCTACCACCTACCCGCCTGGATGGAGTCTCGCTCTGTGCGCCAGGCTGGAG  
TGCAGTGGCACGATCTCGGCTCACTGCAACCTCCGCCTCCCGGGTTCAAGCGAGTCTCTGCG  
CTCAGCCTCTGAGTGTCTGGGGCTACAGGTGCCTGCAGGAGTCTTGGGGCCAGCTGGCCTCG  
ATGTACGTACGACGCGCGGGAACGGTACAAGTGGCTGCGCTTCAGCGAGGACTGTCTGTACCT  
GAACGTGTACGCGCGCGCGCGCGCGCCCGGGGATCCCCAGCTGCCAGTGATGGTCTGGTTCC  
CGGGAGGCGCCTTCATCGTGGGCGCTGCTTCTTCGTACGAGGGCTCTGACTTGGCCGCCCCG  
GAGAAAGTGGTGCTGGTGTCTTCTGCAGCACAGGCTCGGCATCTTCGGCTTCTTGAGCACGGA  
CGACAGCCACGCGCGCGGGAACCTGGGGGCTGCTGGACCAGATGGCGGCTCTGCGCTGGGTGC  
AGGAGAACATCGCAGCCTTCGGGGGAGACCCAGGAAATGTGACCCTGTTGGGCCAGTCCGGC  
GGGGCCATGAGCATCTCAGGACTGATGATGACCCCTAGCCTCGGGTCTCTTCCATCGGGC  
CATTTCCAGAGTGGCACCGCGTTATTTCAGACTTTTCATCACTAGTAACCCACTGAAAGTGG  
CCAAGAAGGTTGCCACCTGGCTGGATGCAACCACAACAGCACACAGATCCTGGTAAACTGC  
CTGAGGGCACTATCAGGGACCAAGGTGATGCGTGTGTTCCAACAAGATGAGATTCTTCCAAC  
GAACTTCCAGAGAGACCCGGAAGAGATTATCTGGTCCATGAGCCCTGTGGTGGATGGTGTGG  
TGATCCCAGATGACCCTTTGGTGCTCCTGACCCAGGGGAAGGTTTCATCTGTGCCCTACCTT  
CTAGGTGTCAACAACCTGGAATTCAATTGGCTCTTGCCCTTATAATATCACCAAGGAGCAGGT  
ACCACTTGTGGTGGAGGAGTACCTGGACAATGTCAATGAGCATGACTGGAAGATGCTACGAA  
ACCGTATGATGGACATAGTTCAAGATGCCACTTTCGTGTATGCCACACTGCAGACTGCTCAC  
TACCACCGAGAAACCCCAATGATGGGAATCTGCCCTGCTGGCCACGCTACAACAAGGATGAA  
AAGTACCTGCAGCTGGATTTTACCACAAGAGTGGGCATGAAGCTCAAGGAGAAGAAGATGGC  
TTTTTGGATGAGTCTGTACCAGTCTCAAAGACCTGAGAAGCAGAGGCAATTCTAAGGGTGGC  
TATGCAGGAAGGAGCCAAAGAGGGGTTTGCCCCCACCATCCAGGCCCTGGGGAGACTAGCCA  
TGGACATACCTGGGGACAAGAGTTCTACCCACCCAGTTTAGAACTGCAGGAGCTCCCTGCT  
GCCTCCAGGCCAAAGCTAGAGCTTTTGCCCTGTTGTGTGGGACCTGCACTGCCCTTTCCAGCC  
TGACATCCCATGATGCCCTCTACTTCACTGTTGACATCCAGTTAGGCCAGGCCCTGTCAAC  
ACCACACTGTGCTCAGCTCTCCAGCCTCAGGACAACCTCTTTTTTTCCCTTCTTCAAATCCT  
CCCACCTTCAATGTCTCCTTGTGACTCCTTCTTATGGGAGGTGACCCAGACTGCCACTGC  
CCCTGTCACTGCACCCAGCTTGGCATTACCATCCATCCTGCTCAACCTTGTTCCTGTCTGT  
TCACATTGGCCTGGAGGCCTAGGGCAGGTTGTGACATGGAGCAAACCTTTTGGTAGTTGGGA  
TCTTCTCTCCACCCACACTTATCTCCCCAGGGCCACTCCAAGTCTATACACAGGGGTGG  
TCTCTTCAATAAAGAAGTGTGATTAGAAAAA

**FIGURE 91**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44179  
<subunit 1 of 1, 545 aa, 1 stop  
<MW: 58934, pI: 9.45, NX(S/T): 4  
MSTGFSFGSGTLGSTTVAAGGTSTGGVFSFGTGTSSNPSVGLNFGNLGSTSTPATTSSAPSSG  
FGTGLFGSKPATGFTLGGTNTGALHTKRPQVVTKYGTLOGKQMHVGKTPIQVFLGVFPFSRPP  
LGILRFAPPEPPEPWKGIRDATTYPGWSLALSPGWSAVARSRLTATSASRVQASLLPQPLS  
VWGYRCLQESWGQLASMYVSTRERYKWLRFSEDCLYLNVIYAPARAPGDPQLPVMVWFPGGAF  
IVGAASSYEGSDLAAREKVVLVFLQHRLGIFGFLSTDDSHARGNWGLLDQMAALRWVQENIA  
AFGGDPGNVTLFGQSAGAMSISGLMMSPLASGLFHRAISQSGTALFRLFITSNPLKVAKKVA  
HLAGCNHNSTQILVNCILRALSGTKVMRVSNNKMRFLQLNFQORDPEEIIWSMSPVVDGVVIPDD  
PLVLLTQGKVSSVPYLLGVNNLEFNWLLPYNITKEQVPLVVEEYLDNVNEHDWKMLRNRMMMD  
IVQDATFVYATLQTAHYHRETPMMGICPAGHATTRMKSTCSWILPQEWA

**Important features:**

**Signal peptide:**

amino acids 1-29

**Carboxylesterases type-B serine active site.**

amino acids 312-327

**Carboxylesterases type-B signature 2.**

amino acids 218-228

**N-glycosylation sites.**

amino acids 318-321, 380-383 and 465-468



**FIGURE 93**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA54002  
><subunit 1 of 1, 544 aa, 1 stop  
><MW: 60268, pI: 9.53, NX(S/T): 3  
MLLP LLLSSLLGGSQAMDGRFWIRVQESVMVPEGLCISVPCSF SYPRQDWTGSTPAYGYWFK  
AVTETTKGAPVATNHQSREVE MSTRGRFQLTGDPKAGNCSLVIRDAQM QDESYFFERVERGS  
YVTYNFMNDGFFLKVTVLSFTPRPDHNTDLTCHVDFSRKGVSAQRTVRLRVAYAPRDLVIS  
ISRDNTPALEPQPQGNVPYLEAQKGQFLRLLCAADSQPPATLSWVLQNRVLSSSHPWGPRPL  
GLELPGVKAGDSGRYTCRAENRLGSQQRALDLSVQYPPENLRVMVSQANRTVLENLNGTSL  
PVLEGQSLCLVCVTHSSPPARLSWTQRGQVLSPSQPSDPGVLELPRVQVEHEGEFTCHARHP  
LGSQHVSLSLSVHYKKGLISTAFSNGAFLGIGITALLFLCLALIIMKILPKRRTQTETPRPR  
FSRHSTILDYINVVPTAGPLAQKR NQKATPNSPRTPPPPGAPSPESKKNQKKQYQLPSFPEP  
KSSTQAPESQESQEELHYATLNFP GVRPRPEARMPKGTQADYAEVKFQ

**Important features:****Signal peptide:**

amino acids 1-15

**Transmembrane domain:**

amino acids 399-418

**N-glycosylation site.**

amino acids 100-103, 297-300 and 306-309

**Immunoglobulins and major histocompatibility complex proteins signature.**

amino acids 365-371

**FIGURE 94**

TGAAGAGTAATAGTTGGAATCAAAAGAGTCAACGCAATGAACTGTTATTTACTGCTGCGTTT  
TATGTTGGGAATTCCTCTCCTATGGCCTTGCTTGGAGCAACAGAAAACCTCTCAAACAAAGA  
AAGTCAAGCAGCCAGTGGGATCTCATTGAGAGTGAAGCGTGGCTGGGTGTGGAACCAATTT  
TTTGTACCAGAGGAAATGAATACGACTAGTCATCACATCGGCCAGCTAAGATCTGATTTAGA  
CAATGGAAACAATTCTTTCCAGTACAAGCTTTTGGGAGCTGGAGCTGGAAGTACTTTTATCA  
TTGATGAAAGAACAGGTGACATATATGCCATACAGAAGCTTGATAGAGAGGAGCGATCCCTC  
TACATCTTAAGAGCCCAGGTAATAGACATCGCTACTGGAAGGGCTGTGGAACCTGAGTCTGA  
GTTTGTTCATCAAAGTTTCGGATATCAATGACAATGAACCAAAATTCCTAGATGAACCTTATG  
AGGCCATTGTACCAGAGATGTCTCCAGAAGGAACATTAGTTATCCAGGTGACAGCAAGTGAT  
GCTGACGATCCCTCAAGTGGTAATAATGCTCGTCTCCTCTACAGCTTACTTCAAGGCCAGCC  
ATATTTTTCTGTTGAACCAACAACAGGAGTCATAAGAAATATCTTCTAAAATGGATAGAGAAC  
TGCAAGATGAGTATTGGGTAATCATTCAAGCCAAGGACATGATTGGTCAGCCAGGAGCGTTG  
TCTGGAACAACAAGTGTATTAATTAACCTTTTCAGATGTTAATGACAATAAGCCTATATTTAA  
AGAAAGTTTATACCGCTTGACTGTCTGTAATCTGCACCCACTGGGACTTCTATAGGAACAA  
TCATGGCATATGATAATGACATAGGAGAGAATGCAGAAATGGATTACAGCATTGAAGAGGAT  
GATTCGCAAAACATTTGACATTATTACTAATCATGAAACTCAAGAAGGAATAGTTATATTTAA  
AAAGAAAGTGGATTTTGGACACCAGAACCCTACGGTATTAGAGCAAAAGTTAAAAACCATC  
ATGTTCCCTGAGCAGCTCATGAAGTACCACACTGAGGCTTCCACCCTTTTCATTAAGATCCAG  
GTGGAAGATGTTGATGAGCCTCCTCTTTTCCCTCCTTCCATATTATGTTTTGAAGTTTTTGA  
AGAAACCCACAGGGATCATTTGTAGGCGTGGTGTCTGCCACAGACCCAGACAATAGGAAAT  
CTCCTATCAGGTATTCTATTACTAGGAGCAAAGTGTTCAATATCAATGATAATGGTACAATC  
ACTACAAGTAACTCACTGGATCGTGAAATCAGTGCTTGGTACAACCTAAGTATTACAGCCAC  
AGAAAAATACAATATAGAACAGATCTCTCGATCCCACTGTATGTGCAAGTTCTTAACATCA  
ATGATCATGCTCCTGAGTTCTCTCAATACTATGAGACTTATGTTTGTGAAAATGCAGGCTCT  
GGTCAGGTAATTCAGACTATCAGTGCAGTGGATAGAGATGAATCCATAGAAGAGCACCATTT  
TTACTTTAATCTATCTGTAGAAGACACTAACAATTCAGTTTACAATCATAGATAATCAAG  
ATAACACAGCTGTCAATTTGACTAATAGAAGCTGGTTTTAACCTTCAAGAAGAACCTGTCTTC  
TACATCTCCATCTTAATTGCCGACAATGGAATCCCGTCACTTACAAGTACAAACACCCTTAC  
CATCCATGTCTGTGACTGTGGTGACAGTGGGAGCACACAGACCTGCCAGTACCAGGAGCTTG  
TGCTTTCCATGGGATTCAAGACAGAAGTTATCATTGCTATTCTCATTGTCATTATGATCATA  
TTTGGGTTTTATTTTTTTGACTTTGGGTTTTAAACAACGGAGAAAACAGATTCTATTTCTGA  
GAAAAGTGAAGATTTAGAGAGAATATATCCAATATGATGATGAAGGGGGTGGAGAAGAAG  
ATACAGAGGCCTTTGATATAGCAGAGCTGAGGAGTAGTACCATAATGCGGGAACGCAAGAG  
CGGAAAACCACAAGCGCTGAGATCAGGAGCCTATACAGGCAGTCTTTGCAAGTTGGCCCCGA  
CAGTGCCATATTCAGGAAATTCATTCTGGAAAAGCTCGAAGAAGCTAATACTGATCCGTGTG  
CCCCTCCTTTTGATTCCCTCCAGACCTACGCTTTTGAGGGAACAGGGTCATTAGCTGGATCC  
CTGAGCTCCTTAGAATCAGCAGTCTCTGATCAGGATGAAAGCTATGATTACCTTAATGAGTT  
GGGACCTCGCTTTAAAAGATTAGCATGCATGTTTGGTTCTGCAGTGCAGTCAAATAATTAGG  
GCTTTTTTACCATCAAAATTTTTAAAAGTGCTAATGTGTATTTCGAACCCAATGGTAGTCTTAA  
AGAGTTTGTGCCCTGGCTCTATGGCGGGGAAAGCCCTAGTCTATGGAGTTTTCTGATTTCC  
CTGGAGTAAATACTCCATGGTTATTTTAAAGCTACCTACATGCTGTCATTGAACAGAGATGTG  
GGGAGAAATGTAAACAATCAGCTCACAGGCATCAATACAACCAGATTTGAAGTAAAATAATG  
TAGGAAGATATTAAAAGTAGATGAGAGGACACAAGATGTAGTCGATCCTTATGCGATTATAT  
CATTATTTACTTAGGAAAGAGTAAAAATACCAAACGAGAAAATTTAAAGGAGCAAAAATTTG  
CAAGTCAAATAGAAATGTACAAATCGAGATAACATTTACATTTCTATCATATTGACATGAAA  
ATTGAAAATGTATAGTCAGAGAAATTTTCATGAATTATTCCATGAAGTATTGTTTCCTTTAT  
TTAAA

**FIGURE 95**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA53906

><subunit 1 of 1, 772 aa, 1 stop

><MW: 87002, pI: 4.64, NX(S/T): 8

MNCYLLLRFMLGIPLLWPCLGATENSQTKKVKQPVRSHLRVKGWVWNQFFVPEEMNTTSHH  
IGQLRSDLNNGNNSFOYKLLGAGAGSTFIIDERTGDIYAIQKLDREERSLYILRAQVIDIAT  
GRAVEPESEFVIKVSNDINDNEPKFLDEPYEAIVPEMSPEGTLVIQVTASDADDPSSGNNARL  
LYSLLQGQPYFSVEPTTGIVIRISSKMDRELQDEYWVIIQAKDMIGQPGALSGTTSVLIKLSD  
VNDNKPIFKESLYRLTVSESAPTGTSGITIMAYDNDIGENAEMDYSIEEDDSQTFDIITNHE  
TQEGIVILKKKVD FEHQNHYGIRAKVKNHHVPEQLMKYHTEASTTFIKIQVEDVDEPPLFLL  
PYYVFEVFEETPQGSFVGVSATDPDNRKSPIRYSITRSKVFENINDNGTITTSNSLDREISA  
WYNLSITATEKYNIEQISSIPLYVQVLNINDHAPEFSQYYETYVCENAGSGQVIQTISAVDR  
DESIEEHFFYFNLSVEDTNSSFTIIDNQDNTAVILTNRTGFNLQEEPVFYISILIADNGIP  
SLTSTNTLTIHVCDGSGSTQTCQYQELVLSMGFKTEVIIAILICIMIIIFGFIFLTLGLKQ  
RRKQILFPEKSEDFRENIFQYDDEGGGEEDTEAFDIAELRSSTIMRERKTRKTTSAEIRSLY  
RQSLQVGPDSAIFRKFILEKLEEANTDPCAPPFDSLQTYAFEGTGS LAGSLSSLES AVSDQD  
ESYDYLNELGPRFKRLACMFGSAVQSNN

**Important features:**

**Signal peptide:**

amino acids 1-21

**Transmembrane domain:**

amino acids 597-617

**N-glycosylation sites.**

amino acids 57-60, 74-77, 419-423, 437-440, 508-511, 515-518,  
516-519 and 534-537

**Cadherins extracellular repeated domain signature.**

amino acids 136-146 and 244-254

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**FIGURE 96**

ATTTCAAGGCCAGCCATATTTTTNTGTTGAACCAACAACAGGAGTCATAAGAATATTTNTA  
AAATGGATAGAGAACTGCAAGATGAGTATTGGGTAATCATTCAAGCCAAGGACATGATTGGT  
CAGCCAGGAGCGTTGTNTGGAACAACAAGTGTATTAATTAACTTTCAGATGTTAATGACAA  
TAAGCCTATATTTAAAGAAAGTTTATACCGCTTGACTGTNTNTGAATCTGCACCCACTGGGA  
NTTNTATAGGAACAATCATGGCATATGATAATGACATAGGAGAGAATGCAGAAATGGATTAC  
AGCATTGAAGAGGATGATTGCGCAAACATTGACATTATT

**FIGURE 97**

GCAACCTCAGCTTCTAGTATCCAGACTCCAGCGCCGCCCCGGGCGCGGACCCCAACCCCGAC  
CCAGAGCTTCTCCAGCGGGCGCGCAGCGAGCAGGGCTCCCCGCCTTAACCTCCTCCGCGGGG  
CCCAGCCACCTTCGGGAGTCCGGGTGCCCACCTGCAAACTCTCCGCCTTCTGCACCTGCCA  
CCCCTGAGCCAGCGCGGGCCCCCGAGCGAGTCATGGCCAACGCGGGGCTGCAGCTGTTGGGC  
TTCATTCTCGCCTTCTGGGATGGATCGGCGCCATCGTCAGCACTGCCCTGCCCCAGTGGAG  
GATTTACTCCTATGCCGGCGACAACATCGTGACCGCCAGGCCATGTACGAGGGGCTGTGGA  
TGTCCTGCGTGTCGCAGAGCACCGGGCAGATCCAGTGCAAAGTCTTTGACTCCTTGCTGAAT  
CTGAGCAGCACATTGCAAGCAACCCGTGCCTTGATGGTGGTTGGCATCCTCCTGGGAGTGAT  
AGCAATCTTTGTGGCCACCCTTGGCATGAAGTGTATGAAGTGCTTGAAGACGATGAGGTGC  
AGAAGATGAGGATGGCTGTATTGGGGGTGCGATATTTCTTCTTGACGGTCTGGCTATTTTA  
GTTGCCACAGCATGGTATGGCAATAGAATCGTTCAAGAATTCTATGACCCATGACCCCACT  
CAATGCCAGGTACGAATTTGGTCAGGCTCTCTTCACTGGCTGGGCTGCTGCTTCTCTGCT  
TTCTGGGAGGTGCCCTACTTTGCTGTTCTGTCCCCGAAAAACAACCTCTTACCCAACACCA  
AGGCCCTATCCAAAACCTGCACCTTCCAGCGGGAAAGACTACGTGTGACACAGAGGCAAAAG  
GAGAAAATCATGTTGAAACAAACCGAAAATGGACATTGAGATACTATCATTAACATTAGGAC  
CTTAGAATTTTGGGTATTGTAATCTGAAGTATGGTATTACAAAACAAACAAACAAACAAAA  
ACCCATGTGTTAAAATACTCAGTGCTAAACATGGCTTAATCTTATTTTATCTTCTTCTCA  
ATATAGGAGGGAAGATTTTCCATTTGTATTACTGCTTCCCATTGAGTAATCATACTCAAAT  
GGGGGAAGGGGTGCTCCTTAAATATATATAGATATGTATATATACATGTTTTTCTATTAAAA  
ATAGACAGTAAATACTATTCTCATTATGTTGATACTAGCATACTTAAATATCTCTAAAT  
AGGTAAATGTATTTAATCCATATTGATGAAGATGTTTATTGGTATATTTTCTTTTCGTCC  
TTATATACATATGTAACAGTCAAATATCATTACTCTTCTTCAATTAGCTTTGGGTGCCTTTG  
CCACAAGACCTAGCCTAATTTACCAAGGATGAATCTTTCAATTCCTCATGCGTGCCCTTTT  
CATATACTATTTTATTTTACCATAATCTTATAGCACTTGCCATCGTTATTAAGCCCTTAT  
TTGTTTTGTGTTTCAATTGGTCTCTATCTCCTGAATCTAACACATTCATAGCCTACATTTTA  
GTTTCTAAAGCCAAAGAATTTATTACAAATCAGAACTTTGGAGGCAATCTTCTGCATG  
ACCAAAGTGATAAATTCCTGTTGACCTCCCACACAATCCCTGTACTCTGACCCATAGCACT  
CTTGTTTGCTTTGAAAATATTTGTCCAATTGAGTAGCTGCATGCTGTTCCCCAGGTGTTGT  
AACACAACCTTTATTGATTGAATTTTAAAGCTACTTATTCAAGTTTTATATCCCCCTAACT  
ACCTTTTTGTTCCCCATTCTTAATTGTATTGTTTTCCCAAGTGTAATTATCATGCGTTTTA  
TATCTTCCTAATAAGGTGTGGTCTGTTTGTCTGAACAAAGTGCTAGACTTTCTGGAGTGATA  
ATCTGGTGACAAATATTCTCTCTGTAGCTGTAAGCAAGTCACTTAATCTTTCTACCTCTTTT  
TTCTATCTGCCAAATTGAGATAATGATACTTAACCAAGTTAGAAGAGGTAGTGTGAATATTAA  
TTAGTTTATATTACTCTTATTCTTTGAACATGAACATATGCCTATGTAGTGTCTTTATTTGCT  
CAGCTGGCTGAGACACTGAAGAAGTCACTGAACAAAACCTACACACGTACCTTCATGTGATT  
CACTGCCTTCTCTCTCTACCAGTCTATTTCCACTGAACAAAACCTACACACATACCTTCAT  
GTGGTTCAGTGCCTTCTCTCTCTACCAGTCTATTTCCACTGAACAAAACCTACGCACATAC  
CTTCATGTGGCTCAGTGCCTTCTCTCTCTACCAGTCTATTTCCATTCTTTAGCTGTGTCT  
GACATGTTTGTGCTCTGTTCATTTTAACTGCTCTTACTTTTCCAGTCTGTACAGAATG  
CTATTTCACTTGAGCAAGATGATGTAATGGAAGGGTGTGGCACTGGTGTCTGGAGACCTG  
GATTTGAGTCTTGGTGCTATCAATCACCGTCTGTGTTTGAGCAAGGCATTTGGCTGCTGTAA  
GCTTATTGCTTCATCTGTAAGCGGTGGTTTGAATTCCTGATCTTCCACCTCACAGTGATG  
TTGTGGGGATCCAGTGAGATAGAATACATGTAAGTGTGGTTTTGTAATTTAAAAAGTGCTAT  
ACTAAGGGAAAGAATTGAGGAATTAAGTGCATACGTTTTGGTGTTGCTTTTCAAATGTTTGA  
AAATAAAAAAATGTTAAG



**FIGURE 98**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA52185

><subunit 1 of 1, 211 aa, 1 stop

><MW: 22744, pI: 8.51, NX(S/T): 1

MANAGLQLLGFI LAFLGWIGAIVSTALPQWRIYSYAGDNIVTAQAMYEG LWMSCVSQSTGQI  
QCKVFDSLNLNLSSTLQATRALMVVGILLGVIAIFVATVGMKCMKCLEDDDEVQKMRMAVIGGA  
IFLLAGLAILVATAWYGNRIVQEFYDPMTPVNARYEFGQALFTGWAAASLCLLGGALLCCSC  
PRKTTSYPTPRPYPKPAPSSGKD YV

**Important features:**

**Signal peptide:**

amino acids 1-21

**Transmembrane domains:**

amino acids 82-102, 118-142 and 161-187

**N-glycosylation site.**

amino acids 72-75

**PMP-22 / EMP / MP20 family proteins**

amino acids 70-111

**ABC-2 type transport system integral membrane protein**

amino acids 119-133

**FIGURE 99**

TTCTGGCCAAACCCGGGGCTNCAGCTGTTGGGCTTCATCTCGCCTTCCTGGGATGGATCGGC  
GCCATCNTCACACTGCCCTTCCCCAGTGGAGGATTTTACTCCCTATGCTGGCGACAACATCG  
TGACCGCCCAGCCCATGTACGAGGGGCTGTGGATGTCCNGCGTGTGCGAGAGCACCGGGCAG  
ATCCAGTGCAAAGTCTTTGACTCCTTGCTGAATCTGAGCAGCACATTGCAAGCAACCCGTGC  
CTTGATGGTGGTTGGCATCCTCCTGGGAGTGATAGCAATCTTTGTGGCCACCGTTGGCATGA  
AGTGTATGAAGTGCTTGGAAGACGATGAGGTGCAGAAGATGAGGATGGCTGTCATTGGGGGC  
GCGATATTTCTTCTTGCAAGGTCTGGCTATTTTAGTTGCCACAGCATGGTATGGCAATAGAAN  
CNTTCAACANTTCTATGACCCTATGACCCAGTCAATGCCAGGTACGAATTTGGTCA  
GGCTCTCTTCACTGGCTGGGCTGCTGCTTCTCTGCCTTCTGGGAGGTGCCCTACTTTGCT  
GTTCTGTCCC

**FIGURE 100**

ACCCTTGACCCAACGCGGCCCCCGACCGNTTCATGGCCAAACGCGGGNCTCCAGCTGTTGG  
GCTTCATTCTCCCCCTTCCTGGGATGGACCGGCGCCATCNTCAGCACTGCCCTGCCCCAGTG  
GAGGATTTACTCCTATNCCGGCNACAACATCGTGACCGCCCAGGCCNTGTACGAGGGGCTGT  
GGATGTCCTGCGTGTCGCAGAGCACCGGGCAGATCCAGTGCAAAGTCTTTGACTCCCTTGCT  
GAATCTGAGCAGCACATTGCAAGCAACCCGTGCCTTGATGGTGGTTGGCATCCTCCTGGGAG  
TGATAGCAATCTTNNTGGCCACCGTTGTNNNTGAAGTGTATGAAGTGCTTGGAAGACGATGA  
GGTGCAGAAGATGAGGATGGCTGTCATTGGGGGCGCGATATTTCTTCTTGCAAGTCTGGCTA  
TTTAGTTGCCACAGCATGGTATGGCAATAGAATCGTTCAAGAATTCTATGACCCTATGACCGA

**FIGURE 101**

GGGCCCCGACCATTATCCAACCGGGNTCACTGTTGGCTCATCTCCCTCCTGGATGAANCGCGC  
CATCNTCAGACTCCCTGCCCCATGGAGATTTNNCCTATGCTGGCGACAACATCNTGACCCCC  
AGCCATGTACGAGGGGCTTTGAACGTCNGCGTGTCGCAGANCACCGGGCAGATCCAGTGCAA  
AGTCTTTGACTCCTTGCTGAATCTGNGCAGCACATTGCAGCAACCCNTGCCCTGATGGTGGT  
TGGCATCCTCCTGGGAGTGATAGCAATCTTTGTGGCCACCGTTGGCATGAAGTGTATGAAGT  
GCTTGGAAGACGATGAGGTGCAGAAGATGAGGATGGCTGTCATTGGGGGCGCGATATTTCTT  
CTTGCAAGTCTGGCTATTTNNNGTTGCCACAGCATGGTATGGCAATAGAATCGTTCAAGAAT  
TCTATGACCCTATGACCCCAGTCAATGCCAGGTACGAATTTGGTCAGGCTCTCTTCACTGGC  
TGGGCTGCTGCTTCTCTCTGCCTTCTGGGAGGTGCCCTACTTTGCTGTTCTCCTGCGA

**FIGURE 102**

ATTCTCCCCTCCTGGATGGATCGCNCCACCGTCACATTGCCTTCCCCCANTGGAGGATTNAC  
TCCTATGCTGGCGACAACATCGTGACCCCCCAGGCCATTTACCGAGGGGCTTTGGATGTCNT  
GCNTGTCGCAGAGCACCGGGCAGATCCCAGTGCAAAGTCTTTGACTCCTTGCTGAATCTGAG  
CAGCACATTGCAAGCAACCCGTGCCTTGATGGGGTTGGCATCCTCCTGGGAGTGATAGCAAC  
CTTTGTGGCCACCGTTGGCATGAAGTGTATGAAGTGCTTGAAGACGATGAGGTGCCAGAAG  
ATGAGGATGGCTGTCATTGGGGGCGCGATATTTCTTGTTGCAGGTCTGGCTATTTTAGTNGC  
CACAGCATGGTATGGCAATAGANTNNTTCNNGNNNTCTATGACCCTATGACCCCAGTCAATG  
CCAGGTACGAATTTGGTCAGGCTCTCTTCACTGGCTGGGCTGCTGCTTCTCTCTGCCTTCTG  
GGAGGTGCCCTACTTTGCTGTTCTGTCCC

**FIGURE 103**

AGAGCACCGGCAGATCCCAGTNCAAAGTCTTTGACCCTTGCTGAATCTGAGCAGCACATTNC  
AAGCAACCCCTTGCCTTGAAGGTGGTTGNCATCCCCCTGGGAGTGAATAGCAATCTTTGTG  
GCCACCGTTGGCATGAAGTNTATGAAGTGCTTGAAGACGATGAGGTGCAGAAGATGAGGAT  
GGCTGTCATTGGGGGCGCGATATTTCTTCTTGACGGTCTGGCTATTTTAGTNNCCACAGCAT  
GGTATGGCAATAGNATNNTTCGNNGGNTTCTATGACCCTATGACCCAGTCAATGCCAGGTAC  
GAATTTGGTCAGGCTCTCTTCACTGGCTGGGCTGCTGCTTCTCTCTGCCTTCTGGGAGGTGC  
CCTACTTTGCTGTTCTGTCCCCGAA

**FIGURE 104**

AGCAATGCCCTGCCCCCAGTGGAGGATTAATTCCTATGNTGGGGACAACATTGTGACNGCCC  
AGGCCATGTACGGGGGGCTGTGGATGTCCTGCGTGTGCGCAGAGCACCGGGCAGATCCAGTGC  
AAAGTNTTTGACTCCTTGCTGAATTTGAGCAGCACATTGCAAGCAACCCGTGCCTTGATGGT  
GGTTGGCATCTTCCTGGGAGTGATAGCAATCTTTGTGGCCACCGTGGNAATGAAGTGTATGA  
AGTGCTTGGAAGACGATGAGGTGCAGAAGATGAGGATGGCTGTCATTGGGGGCGCGATATTT  
CTTNTTGCAGGTCTGGCTATTTTAGTTGCCACAGCATGGTATGGCAATAGAATNGTTCAAGA  
ATTTTATGACCCTATGACCCCAAGTCAATGCCAGGTACGAATTTGGTCAGGCTTTNTTCACTG  
GCTGGGCTGCTGCTTNTTCTGCCTTNTGGGAGGTGCCCTANTTTGCTGTTTCTGCGAACC

## FIGURE 105

TCATAGGGGGGCGCGATATTTTTCTTGCAGGTNTGGTTATTTTAGTTGCCACAGCATGGTA  
TGGCAATAGAATCGTTCAAGAATTNTATGACCCTATGACCCAGTCAATGCCAGGTACGAAT  
TTGGTCAGGCTCTNTTCACTGGNTGGGCTGCTGCTTCTNTNNGCCTTNTGGGAGGTGCCCTA  
CTTTGCTGTTTCCTG



**FIGURE 106**

TTCCTGGGATGGATCCGCCCCATCNTCACATGCCCTGCCCCNTGGAGATTTACNCCTATGC  
TGGCGAACAACATCNTGACCGCCCAGGCCATGTACGAGGGGCTGTGGAATGTCCTGCGTGTC  
CCAGAGCACCGGGCAGATCCAGTGCAAAGTCTTTGACTCCTTGCTGAATCTGAGCAGCACAT  
TGCAAGCAACCNTGCCTTGATGGTGGTTGGCATCCTCCTGGGAGTGATAGCAATCTTTGTGG  
CCACCGTTGGCATGAAAGTGTATGAAGTGCTTGGAAGACGATGAGGTGCAGAAGATGAGGAT  
GGCTGTCATTGGGGGCGCGATATTTCTTCTTGCAAGTCTGGCTATTTTAGNNGCCACAGCAT  
GGTATGGCAATCAGACCCNNTCANAACTCTATGACCCTATGACCCAGTCAATGCCAGGTA  
CGAATTTGGTCAGGCTCTCTTCACTGGCTGGGCTGCTGCTTCTCTCTGCCTTCTGGGAGGTG  
CCCTACTTTGCTGTTCTGTCCCCGAAAAACAACCTCTTACCCACG

**FIGURE 107**

CGGGGCTGCAGCTGTTGGGCTTCATCTCGCTTCCTGGGATGGAATCGGCGCCATCGTCAGCA  
CTGCCCTGCCCCATGGAGGATTTACTCNTATGCTGGCGACAACATCGTGACCNCCCAGGCCA  
TGTACGAGGGGCTGTGGATGTCNGCGTGTGCGAGAGCACCGGGCAGATCCAGTGCAAAGTCT  
TTGACTCCTTGCTGAATCTGAGCAGCACATTGCAAGCAACCNTGCCTTGATGGTGGTTGGCA  
TCCTCCTGGGAGTGATAGCAATCTTTGTGGCCACCGTTGGCATGAAGTGTATGAAGTGCTTG  
GAAGACGATGAGGTGCAGAAGATGAGGATGGCTGTCATTGGGGGCGCGATATTTCTTCTTGC  
AGGTCTGGCTATTTNTAGTTGCCACAGCATGGTATGGCAATAGAATCGTTCAAGAATTCTAT  
GACCCTATGACCCCAGTCAATGCCAGGTACGAATTTGGTCAGGCTCTCTTCACTGGCTGGGC  
TGCTGCTTCTCTCTGCCTTCTGGGAGGTGCCCTACTTTGCTGTTTCCTGCGAA

**FIGURE 108**

GCGTGCCGTCAGCTCGCCGGGCACCGCGGCCTCGCCCTCGCCCTCCGCCCTGCGCCTGCAC  
CGCGTAGACCGACCCCCCTCCAGCGCGCCACCCGGTAGAGGACCCCCGCCCGTGCCCCG  
ACCGGTCCCCGCCTTTTTGTAAACTTAAAGCGGGCGCAGCATTAAACGCTTCCCCGCCCGGT  
GACCTCTCAGGGGTCTCCCCGCCAAAGGTGCTCCGCCGCTAAGGAACATGGCGAAGGTGGAG  
CAGGTCTTGAGCCTCGAGCCGCAGCACGAGCTCAAATTCGAGGTCCCTTCACCGATGTTGT  
CACCACCAACCTAAAGCTTGGCAACCCGACAGACCGAAATGTGTGTTTTAAGGTGAAGACTA  
CAGCACCACGTAGGTACTGTGTGAGGCCCAACAGCGGAATCATCGATGCAGGGGCCTCAATT  
AATGTATCTGTGATGTTACAGCCTTTTCGATTATGATCCCAATGAGAAAAGTAAACACAAGTT  
TATGGTTTCAGTCTATGTTTTGCTCCAACCTGACACTTCAGATATGGAAGCAGTATGGAAGGAGG  
CAAAACCGGAAGACCTTATGGATTCAAACTTAGATGTGTGTTGAATTGCCAGCAGAGAAT  
GATAAACCATGATGTAGAAATAAATAAAATTATATCCACAACCTGCATCAAAGACAGAAAC  
ACCAATAGTGTCTAAGTCTCTGAGTTCCTTCTTGGATGACACCGAAGTTAAGAAGGTTATGG  
AAGAATGTAAGAGGCTGCAAGGTGAAGTTCAGAGGCTACGGGAGGAGAACAAGCAGTTCAG  
GAAGAAGATGGACTGCGGATGAGGAAGACAGTGCAGAGCAACAGCCCCATTTTCAGCATTAGC  
CCCAACTGGGAAGGAAGAAGGCCTTAGCACCCGGCTCTTGGCTCTGGTGTTTGTCTTTA  
TCGTTGGTGTAATTATTGGGAAGATTGCCTTGTAGAGGTAGCATGCACAGGATGGTAAATTG  
GATTGGTGATCCACCATATCATGGGATTTAAATTTATCATAACCATGTGTA AAAAGAAATT  
AATGTATGATGACATCTCACAGGTCTTGCCCTTAAATTACCCCTCCCTGCACACATACAC  
AGATACACACACAAATATAATGTAACGATCTTTTAGAAAGTTAAAAATGTATAGTAACTG  
ATTGAGGGGGAAAAAGAATGATCTTTATTAATGACAAGGGAAACCATGAGTAATGCCACAAT  
GGCATATTGTAAATGTCATTTTAAACATTGGTAGGCCTTGGTACATGATGCTGGATTACCTC  
TCTTAAATGACACCCTTCCTCGCCTGTTGGTGCTGGCCCTTGGGGAGCTGGAGCCCAGCAT  
GCTGGGGAGTGCGGTCAGCTCCACACAGTAGTCCCCACGTGGCCCACTCCCGGCCCAGGCTG  
CTTCCGTGTCTTCAGTTCCTGTCCAAGCCATCAGCTCCTTGGGACTGATGAACAGAGTCAGA  
AGCCCAAAGGAATTGCACTGTGGCAGCATCAGACGTACTCGTCATAAGTGAGAGGCGTGTGT  
TGACTGATTGACCCAGCGCTTTGGAAATAAATGGCAGTGCTTTGTTCACTTAAAGGGACCAA  
GCTAAATTTGTATTGGTTCATGTAGTGAAGTCAAACCTGTTATTCAGAGATGTTTAATGCATA  
TTTAACTTATTTAATGTATTTTCATCTCATGTTTTCTTATTGTCAACAAGAGTACAGTTAATGC  
TGCGTGCTGCTGAACCTCTGTTGGGTGAACCTGGTATTGCTGCTGGAGGGCTGTGGGCTCCTCT  
GTCTCTGGAGAGTCTGGTCATGTGGAGGTGGGGTTTATTGGGATGCTGGAGAAGAGCTGCCA  
GGAAGTGTTTTTCTGGGTGAGTAAATAACAACCTGTCATAGGGAGGGAAATTCTCAGTAGTG  
ACAGTCAACTCTAGGTACCTTTTTTAATGAAGAGTAGTCAGTCTTCTAGATTGTTCTTATA  
CCACCTCTCAACCATTACTCACACTTCCAGCGCCCAGGTCCAAGTCTGAGCCTGACCTCCCC  
TTGGGGACCTAGCCTGGAGTCAGGACAAATGGATCGGGCTGCAGAGGGTTAGAAGCGAGGGC  
ACCAGCAGTTGTGGGTGGGGAGCAAGGGAAGAGAGAACTCTTCAGCGAATCCTTCTAGTAC  
TAGTTGAGAGTTTGACTGTGAATTAATTTATGCCATAAAAGACCAACCCAGTTCTGTTTGA  
CTATGTAGCATCTTGAAAAGAAAAATTATAATAAAGCCCCAAAATTAAGAAAA

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**FIGURE 109**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA53977

<subunit 1 of 1, 243 aa, 1 stop

<MW: 27228, pI: 7.43, NX(S/T): 2

MAKVEQVLSLEPQHELKFRGPFTDVVTTNLKLGNPTRNVCFKVKTTAPRRYCVRPNSGIID  
AGASINVSVM LQPFDYDPNEKSKHKFMVQSMFAPTDTS DMEAVWKEAKPEDLMDSKLRVFE  
LPAENDKPHDVEINKIISTTASKTETPIVSKSLSSSLDDTEVKKVMEECKRLQGEVQRLREE  
NKQFKEEDGLRMRKTVQSNPISALAPTGKEEGLSTRLLALVVLEFFIVGVIIGKIAL

**Important features:**

**Putative transmembrane domain:**

amino acids 224-239

**N-glycosylation site.**

amino acids 68-71

**N-myristoylation site.**

amino acids 59-64, 64-69 and 235-240

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**FIGURE 110**

GTCAGTCTTCTAGATTGTCCTTATCCACCTTTCAACCANTACTCACATTCNAGCGCCCAG  
GTCCANGTCTGAGCCTGACTTCCCCCTGGGGACCTAGCCTGGAGTCAGGACAATGGNTCGGG  
CTGCAGAGGNTTAGAAGCGAGGGCACCAGCAGTTTTGGGTGGGGAGCAAGGGNNGAGAGAAA  
CTCTTCAGCGAATCCTTCTAGTACTAGTTGAGAGTTTGACTGTGAATTAATTTTATGCCATA  
AAAGACNAACCCAGTTCTGTTTGACTATGTAGCATCTTGAAAAGAAAATTATAATAAGCC  
CCAAAATTAAGAATTCTTTTGTCAATTTTGTACATTTGCTCTATGGGGGGAATTATTATTTT  
ATCATTTTTATTATTTTGCCATTGGAAGGTTAACTTTAAAATGAGC

**FIGURE 111**

TATTGTAAAGGCCATTTTAAACCATTGGTAGGCCTTGGTACATGATGCTGGATTACCTCCTT  
AAATGACACCNTTCCTCGCCTGTTGGTGCTGGCCNTTGGGGAGCTGGAGCCCCAGCATGCTG  
GGGAGTGCGGTCAGCTCCACACAGTAGTCCCCACGTGGCCCACTCCCGGCCAGGCTGCTTT  
CCGTGTCTTCAGTTCTGTCCAAGCCATCAGCTCCTTGGGACTGATGAACAGAGTCAGAAGCC  
CAAAGGAATTGCCACTGTGGCAGCATCAGACGTACTCGTCATAAGTGAGAGGCGTGTGTTGA  
CTGATTGACCCAGCGCTTTGGAAATAAATGGCAGTGCTTTGTTCACTTAAAGGGACCAAGCT  
AAATTGTATTGGTTCATGTAGTGAAGTCAAAGTGTATTTCAGAGATGTTTAATGCATATTTA  
ACTTATTTAATGTATTTTCATCTCATGTTTTCTTATTGTCACAAGAGTACAGTTAATGCTGCG  
TGCTGCTGAAGTCTGTTGGGTGAACTGGTATTGCTGCTGGAGGGCTG

**FIGURE 112**

CCCTGGTGGTTTTGTTCTTTAATTCGTTGGTGTAATTNTTGGGAAGATTGCTTGTAGAGGTA  
GNATGCACCNGGCTGGTAAATTGGATTGGTGGATCCACCATATCCATGGGATTTAAATTTAT  
CATAACCATGTGTAAAAAGAAATTAATGTATGATGACATNTCACAGGTATTGCCTTTAAATT  
ACCCATCCCTGNANACACATACACAGATACACANANACAAATNTAATGTAACGATNTTTTAG  
AAAGTTAAAAATGTATAGTAAC

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**FIGURE 113**

GGTGGCCCATTCCTGGCCAGGCTGCTTCCGGTNTTCAGTTCTGTCCAAGCCATCAGCTCC  
TTGGGACTGATGAACAGAGTCAGAAGCCCAAAGGAATTGCACTGTGGCAGCATNAGACGTAC  
TTGTNATAAGTGAGAGGCGTGTGTTGACTGATTGACCCAGCGCTTTGGAAATAAATGGCAGT  
GCTTTGTTTCANTTAAAGGGACCAAGCTAAATTTGTATTGGTTCATGTAGTGAAGTCAAACGTG  
TTATTCAGAGATGTTTAATGCATATTTAANTTATTTAATGTATTTNATNTCATGTTTTCTTA  
TTGTCACAAGAGTACAGTTAATGCTGCGTGCTGCTGAANTNTGTTGGGTGAACTGGTATTGC  
TGCTGGAGGGCTGTGGGCTCCTCTGTCTTTGGAGAGTCTGGTCATGTGGAGGTGGG

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**FIGURE 114**

TGCTTTCCGTGTCTTCAGTTCTGTCCAAGCCATCAGCTCCTTGGGACTTGATGAACAGAGTC  
AGAAGCCCAAAGGAATTGCACTGTGGCAGCATCAGACGTACTCGTCATAAGTGAGAGGCGTG  
TGTTGACTGATTGACCCAGCGCTTTGGAAATAAATGGCAGTGCTTTGTTCACTTAAAGGGAC  
CAAGCTAAATTTGTATTGGTTCATGTAGTGAAGTCAAAGTGTATTTCAGAGATGTTTAATGC  
ATATTTAACTTATTTAATGTATTTTCATCTCATGTTTTCTTATTGTCACAAGAGTACAGTTAA  
TGCTGCGTGC

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**FIGURE 115**

AAACCTTTAAAAGTTGAGGGGAAAAGAATGATCCTTTATTAATGACAAGGGAAACCNTGNGT  
AATGCCACAATGGCATATTGTAAATGTCATTTTAAACATTGGTAGGCCTTGGTACATGATGC  
TGGATTACCTCTCTTAAAATGACACCCTTCCTCGCCTGTTGGTGCTGGCCCTTGGGGAGCTN  
GAGCCCAGCATGCTGGGGAGTGCGGTCTGCTCCACACAGTAGTCCCCANGTGGCCCAANTCCC  
GGCCAGGCTGCTTTCCGTGTCTTCAGTTCTGTCCAAGCCATCAGCTCCTTGGGANTGATGA  
ACAGAGTCAGAAGCCCCAAGGAATTGCANTGTGGCAGCATCAGANGTANTNGTCATAAGTGA  
GAGGCGTGTGTTGANTGATTGACCCAGCGCTTTGGAAATAAATGGCAGTGCTTTGTTcantt  
AAAGGGNCCAAGNTAAATTTGTATTGGTTCATGTAGTGAAGTCAAANTGTTATTcagagatg  
TTTAATGCATATTTAANTTATTTAATGTATTTcATNTCATGTTTTCTTATTGTCACAAGGGT  
ACAGTTAATGCTGCGTGCTGCTGAANTCTGTTGGGTGAANTGGTATTGCTG

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**FIGURE 116**

GGCCCTTGGGGAGCTGGAGCCCAGCATGCTGGGGAGTGCGGTCAGCTCCACACAGTAGTCCC  
CACGTGGCCCACTCCCGGCCAGGCTGCTTCCGTGTCTTCAGTTCTGTCCAAGCCATCAGC  
TCCTTGGGACTGATGAACAGAGTCAGAAGCCCAAAGGAATTGCACTGTGGCAGCATCAGACG  
TACTCGTCATAAGTGAGAGGCGTGTGTTGACTGATTGACCCAGCGCTTTGGAAATAAATGGC  
AGTGCTTTGTTCACTTAAAGGGACCAAGCTAAATTTGTATTGGTTCATGTAGTGAAGTCAAA  
CTGTTATTCAGAGATGTTTAATGCATATTTAACTTATTTAATGTATTTTCATCTCATGTTTTT  
TTATTGTCACAAGAGTACAGTTAATGCTGCGTGCTGCTGAACTCTGTTGGGTGAACTGGTAT  
TGCTGCTGGAGGGCTGTGGGCTCCTCTGTCTCTGGAGAGTCTGGTCATGTGGAGGTGGG

**FIGURE 117**

GCGAGCTCCGGGTGCTGTGGCCCGGCCCTTGGCGGGGCGGCCCTCCGGCTCAGGCTGGCTGAGA  
GGCTCCCGAGCTGCAGCGTCCCCGCCCGCCTCCTCGGGAGCTCTGATCTCAGCTGACAGTGCC  
CTCGGGGACCAACAAGCCTGGCAGGGTCTCACTTTGTTGCCAGGCTGGAGTTCAGTGCCA  
TGATCATGGTTTACTGCAGCCTTGACCTCCTGGGTTCAAGCGATCCTGCTGAGTAGCTGGGA  
CTACAGGACAAAATTAGAAGATCAAAATGGAAAATATGCTGCTTTGGTTGATATTTTCACC  
CCTGGGTGGACCCTCATTGATGGATCTGAAATGGAATGGGATTTTATGTGGCACTTGAGAAA  
GGTACCCCGGATTGTCAAGTGAAGGACTTTCCATCTCACCAGCCCCGCATTTGAGGCAGATG  
CTAAGATGATGGTAAATACAGTGTGTGGCATCGAATGCCAGAAAGAACTCCCAACTCCCAGC  
CTTCTGAATTGGAGGATTATCTTTCCTATGAGACTGTCTTTGAGAATGGCACCCGAACCTT  
AACCAGGGTGAAAGTTCAAGATTTGGTTCTTGAGCCGACTCAAAATATCACCACAAAGGGAG  
TATCTGTTAGGAGAAAGAGACAGGTGTATGGCACCAGCAGGTTTCAAGCATCTTGGACAAA  
AGGTTCTTAACCAATTTCCCTTTCAGCACAGCTGTGAAGCTTTCCACGGGCTGTAGTGGCAT  
TCTCATTTCCCTCAGCATGTTCTAACTGCTGCCCACTGTGTTTCATGATGGAAAGGACTATG  
TCAAAGGGAGTAAAAGCTAAGGGTAGGGTTGTTGAAGATGAGGAATAAAAGTGGAGGCAAG  
AAACGTCGAGGTTCTAAGAGGAGCAGGAGAGAAGCTAGTGGTGGTGACCAAGAGAGGGTAC  
CAGAGAGCATCTGCAGGAGAGAGCGAAGGGTGGGAGAAGAAGAAAAAATCTGGCCGGGGT  
AGAGGATTGCCGAAGGGAGGCCCTTCCCTTTCAGTGGACCCGGGTCAAGAATACCCACATTCCG  
AAGGGCTGGGCACGAGGAGGCATGGGGGACGCTACCTTGGACTATGACTATGCTCTTCTGGA  
GCTGAAGCGTGCTCACAAAAGAAATACATGGAACCTGGAATCAGCCCAACGATCAAGAAAA  
TGCTTGGTGGAAATGATCCACTTCTCAGGATTTGATAACGATAGGGCTGATCAGTTGGTCTAT  
CGGTTTTCAGTGTGTCCGACGAATCCAATGATCTCCTTTACCAATACTGCGATGCTGAGTC  
GGGCTCCACCGGTTCCGGGGTCTATCTGCGTCTGAAAGATCCAGACAAAAGAATTGGAAGC  
GCAAAATCATTGCGGTCTACTCAGGGCACCAGTGGGTGGATGTCCACGGGGTTCAGAAGGAC  
TACAACGTTGCTGTTCGCATCACTCCCCTAAATACGCCCAGATTTGCCTCTGGATTACGG  
GAACGATGCCAATTGTGCTTACGGCTAACAGAGACCTGAAACAGGGCGGTGTATCATCTAAA  
TCACAGAGAAAACCAGCTCTGCTTACCGTAGTGAGATCACTTCATAGGTTATGCCTGGACTT  
GAACTCTGTCAATAGCATTTCAACATTTTCAAATCAGGAGATTTTCGTCCATTTAAAAAA  
TGTATAGGTGCAGATATTGAACTAGGTGGGCACCTCAATGCCAAGTATATACTCTTCTTTA  
CATGGTGATGAGTTTCATTTGTAGAAAAATTTGTTGCCTTCTTAAAAATTAGACACACTTT  
AAACCTTCAAACAGGTATTATAAATAACATGTGACTCCTTAATGGACTTATCTCAGGGTCC  
TACTCTAAGAAGAATCTAATAGGATGCTGGTTGTGTATTAAATGTGAAATTGCATAGATAAA  
GGTAGATGGTAAAGCAATTAGTATCAGAATAGAGACAGAAAGTTACAACACAGTTTGTACTA  
CTCTGAGATGGATCCATTAGCTCATGCCCTCAATGTTTATATTGTGTTATCTGTTGGGTCT  
GGGACATTTAGTTTGTATTTTTTGAAGAATTACAAATCAGAAGAAAAAGCAAGCATTATAAA  
CAAACTAATAACTGTTTTACTGCTTTAAGAAATAACAATTACAATGTGTATTATTTAAAAA  
TGGGAGAAAAGTTTGTCTATGAAATAAACCTAGTTTAGAAATAGGGAAGCTGAGACATTT  
TAAGATCTCAAGTTTTTATTTAACTAATACTCAAAATATGGACTTTTCATGTATGCATAGGG  
AAGACACTTCACAAATTATGAATGATCATGTGTTGAAAGCCACATTATTTTATGCTATACAT  
TCTATGTATGAGGTGCTACATTTTATAGGACAAAGAATTCTGTAATCTTTTCAAGAAAGAGT  
CTTTTTCTCCTTGACAAAATCCAGCTTTTGTATGAGGACTATAGGGTGAATTCTCTGATTAG  
TAATTTTAGATATGTCCTTTCCTAAAAATGAATAAAATTTATGAATATGA

**FIGURE 118**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA57253

<subunit 1 of 1, 413 aa, 1 stop

<MW: 47070, pI: 9.92, NX(S/T): 3

MENMLLLWLIFFTPGLWTLIDGSEMEWDFMWHLRKVPRIVSERTFHLTSPAFEADAKMMVNTVC  
GIECQKELPTPSLSELEDYLSYETVFENGTRTLTRVKVQDLVLEPTQNITTKGVSRRKRQV  
YGTDSRFSILDKRFLTNFPFSTAVKLSTGCSGILISPQHVLTAAHCVHDGKDYVKGSKKLRV  
GLLKMRNKSGGKKRRGSKRSRREASGGDQREGTREHLQERAKGGRRRKSGRGORIAEGRPS  
FQWTRVKNTHIPKGWARGMGDATLDYDYALLELKRAHKKKYMELGISPTIKKMPGGMIHFS  
GFDNDRADQLVYRFCVSDESNDLLYQYCDAESGSTGSGVYLRLLKDPDKKNWKRKIIAVYSG  
HQWVDVHGVQKDYNAVVRITPLKYAQICLWIHGNDANCAYG

**Important features:**

**Signal peptide:**

amino acids 1-16

**N-glycosylation sites.**

amino acids 90-93, 110-113 and 193-196

**Glycosaminoglycan attachment site.**

amino acids 236-239

**Serine proteases, trypsin family, histidine active site.**

amino acids 165-170

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**FIGURE 119**

AATGTGAGAGGGGCTGATGGAAGCTGATAGGCAGGACTGGAGTGTTAGCACCAGTACTGGAT  
GTGACAGCAGGCAGAGGAGCACTTAGCAGCTTATTCAGTGTCCGATTCTGATTCCGGCAAGG  
ATCCAAGCATGGAATGCTGCCGTCGGGCAACTCCTGGCACACTGCTCCTCTTTCTGGCTTTT  
CTGCTCCTGAGTTCCAGGACCGCACGCTCCGAGGAGGACCGGGACGGCCTATGGGATGCCTG  
GGGCCCATGGAGTGAATGCTCACGCACCTGCGGGGGAGGGGCCTCCTACTCTCTGAGGCGCT  
GCCTGAGCAGCAAGAGCTGTGAAGGAAGAAATATCCGATACAGAACATGCAGTAATGTGGAC  
TGCCCAACCAGAAGCAGGTGATTTCCGAGCTCAGCAATGCTCAGCTCATAATGATGTCAAGCA  
CCATGGCCAGTTTTATGAATGGCTTCCTGTGTCTAATGACCCTGACAACCCATGTTCACTCA  
AGTGCCAAGCCAAAGGAACAACCCTGGTTGTTGAAGTAGCACCTAAGGTCTTAGATGGTACG  
CGTTGCTATACAGAATCTTTGGATATGTGCATCAGTGGTTTATGCCAAATTGTTGGCTGCGA  
TCACCAGCTGGGAAGCACCGTCAAGGAAGATAACTGTGGGGTCTGCAACGGAGATGGGTCCA  
CCTGCCGGCTGGTCCGAGGGCAGTATAAATCCCAGCTCTCCGCAACCAAATCGGATGATACT  
GTGGTTGCACTTCCCTATGGAAGTAGACATATTGCCTTGTCTTAAAAGGTCCTGATCACTT  
ATATCTGGAAACCAAACCCTCCAGGGGACTAAAGGTGAAAACAGTCTCAGCTCCACAGGAA  
CTTTCCTTGTGGACAATTCTAGTGTGGACTTCCAGAAATTTCAGACAAAGAGATACTGAGA  
ATGGCTGGACCACTCACAGCAGATTTCAATTGTCAAGATTTCGTAACCTCGGGCTCCGCTGACAG  
TACAGTCCAGTTCATCTTCTATCAACCCATCATCCACCGATGGAGGGAGACGGATTTCTTTC  
CTTGCTCAGCAACCTGTGGAGGAGGTTATCAGCTGACATCGGCTGAGTGCTACGATCTGAGG  
AGCAACCGTGTGGTTGCTGACCAATACTGTCACTATTACCCAGAGAACATCAAACCCAAACC  
CAAGCTTCAGGAGTGCAACTTGGATCCTTGTCCAGCCAGTGACGGATACAAGCAGATCATGC  
CTTATGACCTCTACCATCCCCTTCCTCGGTGGGAGGCCACCCCATGGACCGGTGCTCCTCC  
TCGTGTGGGGGGGGCATCCAGAGCCGGGCAGTTTCCTGTGTGGAGGAGGACATCCAGGGGCA  
TGTCACCTCAGTGGAAGAGTGGAATGCATGTACACCCCTAAGATGCCCATCGCGCAGCCCT  
GCAACATTTTTGACTGCCCTAAATGGCTGGCACAGGAGTGGTCTCCGTGCACAGTGACATGT  
GGCAGGGCCTCAGATACCGTGTGGTCTCTGCATCGACCATCGAGGAATGCACACAGGAGG  
CTGTAGCCCCAAAACAAAGCCCCACATAAAAGAGGAATGCATCGTACCCACTCCCTGCTATA  
AACCCAAAGAGAACTTCCAGTCGAGGCCAAGTTGCCATGGTTCAAACAAGCTCAAGAGCTA  
GAAGAAGGAGCTGCTGTGTGTCAGAGGAGCCCTCGTAAAGTTGTAAAAGCACAGACTGTTCTATA  
TTTGAAACTGTTTTGTTTAAAGAAAGCAGTGTCTCACTGGTTGTAGCTTTCATGGGTTCTGA  
ACTAAGTGTAATCATCTCACCAAAGCTTTTTGGCTCTCAAATTAAAGATTGATTAGTTTCAA  
AAAAAAA

**FIGURE 120**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58847

<subunit 1 of 1, 525 aa, 1 stop

<MW: 58416, pI: 6.62, NX(S/T): 1

MECCRRATPGTLLLFLAFLLLSSRTARSEEDRDGLWDAGPWSECSRTC GGGASYSLRRCLS  
SKSCEGRNIRYRTCSNVDCPPEAGDFRAQQCSAHNDVKHHGQFYEWLPVSNPDNPCSLKCQ  
AKGTTLVVELAPKVLDTGTRCYTESLDMCISGLCQIVGCDHQLGSTVKEDNCGVCNGDGSTCR  
LVRGQYKSQLSATKSDDTVVALPYGSRHIRLVLGPDHLYLETKTLQGTKGENSLSSTGTFL  
VDNSSVDFQKFPDKEILRMAGPLTADFIVKIRNSGSADSTVQFIFYQPIIHRWRETDFPFC  
ATCGGGYQLTSAECYDLRSNRVVADQYCHYYPENIKPKPKLQECNLDPCPASDGYKQIMPYD  
LYHPLPRWEATPWTACSSSCGGGIQSRVSCVEEDIQGHVTSVEEWKCMYTPKMPIAQPCNI  
FDCPKWLAQEWSPCTVTCGQGLRYRVVLCIDHRGMHTGGCSPKTKPHIKEECIVPTPCYKPK  
EKLPVEAKLPWFKQAQAELEEGA AVSEEPS

**Important features:**

**Signal peptide:**

amino acids 1-25

**N-glycosylation site.**

amino acids 251-254

**Thrombospondin 1**

amino acids 385-399

**von Willebrand factor type C domain proteins**

amino acids 385-399, 445-459 and 42-56

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**FIGURE 121**

CGGACGCGTGGGCGGCGGCTGCGGAACTCCCGTGGAGGGGCCGGTGGGCCCTCGGGCCTGAC  
AGATGGCAGTGGCCACTGCGGCGGCAGTACTGGCCGCTCTGGGCGGGGCGCTGTGGCTGGCG  
GCCCCCGGTTTCGTGGGGCCCAGGGTCCAGCGGCTGCGCAGAGGCGGGGACCCCGGCCTCAT  
GCACGGGAAGACTGTGCTGATCACCAGGGGCGAACAGCGGCCCTGGGCCGCGCCACGGCCGCCG  
AGCTACTGCGCCTGGGAGCGCGGGTGATCATGGGCTGCCGGGACCGCGCGCGCGCCGAGGAG  
GCGGCGGGTCAGCTCCGCCGCGAGCTCCGCCAGGCCGCGGAGTGCGGCCCCAGAGCCTGGCGT  
CAGCGGGGTGGGCGAGCTCATAGTCCGGGAGCTGGACCTCGCCTCGCTGCGCTCGGTGCGCG  
CCTTCTGCCAGGAAATGCTCCAGGAAGAGCCTAGGCTGGATGTCTTGATCAATAACGCAGGG  
ATCTTCCAGTGCCCTTACATGAAGACTGAAGATGGGTTTGAGATGCAGTTCGGAGTGAACCA  
TCTGGGGCACTTTCTACTACCAATCTTCTCCTTGGACTCCTCAAAAGTTCAGTCCCAGCA  
GGATTGTGGTAGTTTCTTCCAACTTTATAAATACGGAGACATCAATTTTGATGACTTGAAC  
AGTGAACAAAGCTATAATAAAAGCTTTTGTATAGCCGGAGCAAAGTGGCTAACATTCTTTT  
TACCAGGGAAGTAGCCCGCCGCTTAGAAGGCACAAATGTCACCGTCAATGTGTTGCATCCTG  
GTATTGTACGGACAAATCTGGGGAGGCACATACACATTCCACTGTTGGTCAAACCACTCTTC  
AATTTGGTGTCATGGGCTTTTTTCAAACTCCAGTAGAAGGTGCCCAGACTTCCATTTATTT  
GGCCTCTTCACCTGAGGTAGAAGGAGTGTCAGGAAGATACTTTGGGGATTGTAAAGAGGAAG  
AACTGTTGCCCAAAGCTATGGATGAATCTGTTGCAAGAAAAGTCTGGGATATCAGTGAAGTG  
ATGGTTGGCCTGCTAAAAATAGGAACAAGGAGTAAAAGAGCTGTTTATAAAAGTGCATATCAG  
TTATATCTGTGATCAGGAATGGTGTGGATTGAGAACTTGTTACTTGAAGAAAAAGAATTTTG  
ATATTGGAATAGCCTGCTAAGAGGTACATGTGGGTATTTTGGAGTTACTGAAAAATTATTTT  
TGGGATAAGAGAATTTTCAGCAAAGATGTTTTAAATATATATAGTAAGTATAATGAATAATAA  
GTACAATGAAAAATACAATTATATTGTAAAATTATAACTGGGCAAGCATGGATGACATATTA  
ATATTTGTCAGAATTAAGTGACTCAAAGTGCTATCGAGAGGTTTTTCAAGTATCTTTGAGTT  
TCATGGCCAAAGTGTTAACTAGTTTTACTACAATGTTTGGTGTTTGTGTGGAAATTATCTGC  
CTGGTGTGTGCACACAAGTCTTACTTGAATAAATTTACTGGTAC



**FIGURE 122**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA58747

<subunit 1 of 1, 336 aa, 1 stop

<MW: 36865, pI: 9.15, NX(S/T): 2

MAVATAAAVLAAALGGALWLAARRFVGPRVQRLRRGGDPGLMHGKTVLITGANSGLGRATAAE  
LLRLGARVIMGCRDRARAEEAAGQLRREL RQAAECGPEPGVSGVGELIVRELDLASLRVRA  
FCQEMLQEEPRLDVLINNAGIFQCPYMKTEDGFEMQFGVNHLGHFLLTNLLLGLLKSSAPSR  
IVVVSSKLYKYGDINFDDLNSEQSYNKSFCYSRSKLANILFTRELARRLEGTVNVTNVNLHPG  
IVRTNLGRHIHIPLLVKPLFNLVSWAFFKTPVEGAQTSIYLASSPEVEGVSGRYFGDCKEEE  
LLPKAMDESVARKLWDISEVMVGLLK

**Important features:**

**Signal peptide:**

amino acids 1-21

**Short-chain alcohol dehydrogenase family protein**

amino acids 134-144, 44-56 and 239-248

**N-glycosylation site.**

amino acids 212-215 and 239-242

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**FIGURE 123**

GGGGATTGTAAAGAGGAAGNACTGTGCCCCAAAGNTATGGATGAATCTGTTGCAAGAAAATTN  
TGGGATATCAGTGAAGTGATGGTTNGCCTGCTAAAATAGGAACAAGGAGTAAAAGAGCTGTT  
TATAAACTGCATATCAGTTATATCTGTGATCAGGAATGGTGTGGATTGAGAACTTGTTACT  
TGAAGAAAAAGAATTTTGATATTGGAATAGCCTGNTAAGAGGNACATGTGGGTATTTTGGAG  
TTACTGAAAAATTATTTTGGGATAAGAGAATTTTCAGCAAAGATGTTTTAAATATATATAGT  
AAGTATAATGAATAATAAGTACAATGAAAAATACAATTATATTGTAAAATTATAACTGGGCA  
AGCATGGATGACATATTAATATTTGTCAGAATTAAGTGACTCAAAGTGCTATCGAGAGGTTT  
TTCAAGTATCTTTGAGTTTCATGGCCAAAGTGTTAACTAGTTTTACTACAATGTTTGGTGTT  
TGTGTGGAAATTATCTGCCTGGCTT

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**FIGURE 124**

GAGAGGACGAGGTGCCGCTGCCTGGAGAATCCTCCGCTGCCGTCCGCTCCCGGAGCCCAGCC  
CTTTCCTAACCCAACCCAACCTAGCCCAGTCCCAGCCGCCAGCGCCTGTCCCTGTCACGGAC  
CCCAGCGTTACCATGCATCCTGCCGTCTTCCTATCCTTACCCGACCTCAGATGCTCCCTTCT  
GCTCCTGGTAACTTGGGTTTTTACTCCTGTAACAACCTGAAATAACAAGTCTTGCTACAGAGA  
ATATAGATGAAATTTTAAACAATGCTGATGTTGCTTTAGTAAATTTTTATGCTGACTGGTGT  
CGTTTCAGTCAGATGTTGCATCCAATTTTTGAGGAAGCTTCCGATGTCATTAAGGAAGAATT  
TCCAAATGAAAATCAAGTAGTGTGGCCAGAGTTGATTGTGATCAGCACTCTGACATAGCCC  
AGAGATACAGGATAAGCAAATACCCAACCCTCAAATTGTTTCGTAATGGGATGATGATGAAG  
AGAGAATACAGGGGTGAGCGATCAGTGAAAGCATTGGCAGATTACATCAGGCAACAAAAAG  
TGACCCCATTCAGAAATTCGGGACTTAGCAGAAATCACCCTCTTGATCGCAGCAAAAGAA  
ATATCATTGGATATTTGAGCAAAAGGACTCGGACAACCTATAGAGTTTTTGAACGAGTAGCG  
AATATTTTGCATGATGACTGTGCCTTTCTTTCTGCATTTGGGGATGTTTCAAACCGGAAAG  
ATATAGTGGCGACAACATAATCTACAAACCACCGGCATTCTGCTCCGGATATGGTGTACT  
TGGGAGCTATGACAAATTTGATGTGACTTACAATTGGATTCAAGATAAATGTGTTCTCTT  
GTCCGAGAAATAACATTTGAAAATGGAGAGGAATTGACAGAAGAAGGACTGCCTTTTCTCAT  
ACTCTTTCACATGAAAGAAGATACAGAAAGTTTAGAAATATTCCAGAATGAAGTAGCTCGGC  
AATTAATAAGTGAAAAAGGTACAATAAACTTTTTACATGCCGATTGTGACAAATTTAGACAT  
CCTCTTCTGCACATACAGAAAACCTCCAGCAGATTGTCCTGTAATCGCTATTGACAGCTTTAG  
GCATATGTATGTGTTTGGAGACTTCAAAGATGTATTAATTCCTGGAAAACCTCAAGCAATTCTG  
TATTTGACTTACATTCTGGAAAACCTGCACAGAGAATTCCATCATGGACCTGACCCCACTGAT  
ACAGCCCCAGGAGAGCAAGCCCAAGATGTAGCAAGCAGTCCACCTGAGAGCTCCTTCCAGAA  
ACTAGCACCCAGTGAATATAGGTATACTCTATTGAGGGATCGAGATGAGCTTTAAAAAATTG  
AAAAACAGTTTGTAAGCCTTTCAACAGCAGCATCAACCTACGTGGTGGAAATAGTAAACCTA  
TATTTTCATAATTCTATGTGTATTTTTATTTTGAATAAACAGAAAGAAATTTAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 125**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA57689

<subunit 1 of 1, 406 aa, 1 stop

<MW: 46927, pI: 5.21, NX(S/T): 0

MHPAVFLSLPDLRCSLLLLVTWVFTPVTTEITSLATENIDEILNNADVALVNFYADWCREFSQ  
MLHPIFEEASDVIKEEFPNENQVVFARVDCDQHS DIAQRYRISKYPTLKLFRNGMMMKREYR  
GORSVKALADYIRQOKSDPIQEIRDLAEITTLDRSKRNIIGYFEQKSDNYRVFERVANILH  
DDCAFLSAFGDVSKPERYSGDNIIYKPPGHSAPDMVYLGAMTNFDVTYNWIQDKCVPLVREI  
TFENGEELTEEGLPFLILFHMKEDESLEIFQNEVARQLISEKGTINFLHADCDKFRHPLLH  
IQKTPADCPVIAIDSFRHMYVFGDFKDVLI PGKLKQFVFDLHSGKLHREFHHGPDPTDTAPG  
EQAQDVASSPPRESSFQKLAPSEYRYTLLRDRDEL

**Important features:**

**Signal peptide:**

amino acids 1-29

**Endoplasmic reticulum targeting sequence.**

amino acids 403-406

**Tyrosine kinase phosphorylation site.**

amino acids 203-211

**Thioredoxin family proteins**

amino acids 50-66

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## FIGURE 126

ATTAAGGAAGAATTTCCAAATGAAAATCAAGTAGTNTTTGCCAGAGTNGATTGTGATCAGCA  
CTCTGACATAGCCCAGAGATACAGGATAAGCAAATACCCAACCCTCAAATTGTTTCGTAATG  
GGATGATGATGAAGAGAGAATACAGGGGTCAGCGATCAGTGAAAGCATTGGCAGATTA

**FIGURE 127**

AGAGGCCTCTCTGGAAGTTGTCCCGGGTGTTCGCCGCNNGGAGCCCGGGTCGAGAGGACNAGG  
TGCCGCTGCCTGGAGAATCCTCCGCTGCCGTCGGCTCCCGGAGCCCAGCCCTTTCCTAACCC  
AACCCAACCTAGCCCNGTCCCAGCCGCCAGCGCCTGTCCCTGTCNCGGANCCCAGCGTNACC  
ATGCATCCTGCCGTCTTCCTATCCTTACCCGACCTCAGATGCTCCCTTCTGCTCCTGGTAAC  
TTGGGTTTTTACTCCTGTAACAACCTGAAATAACNNGTCTTGATACNNAGAATATAGATGAAA  
TTTTAAACNATGCTGATGTGGCTTTAGTCAATTTTTATGCTGACTGGTGTCTGTTTCAGTCAG  
ATGTGGCATCCAATTTTTGAGGANGCTTCGATGTCATTAAGGAAGAATTTCCAAATGAAAA  
TCAAGTAGTGTTTGCCAGAGTTGATTGTGATCAGCACTCTGACATAGCCCAGAGATACAGGA  
TAAGCAAATACCCAACCCTCAAATTGTTTCGTAATGGGATGATGATGAAGAGAGAATACAGG  
GGTCAGCGATCAGTGAAAGCATTGGCAGATTACATCAGGC

**FIGURE 128**

GCCCACGCGTCCGATGGCGTTCACGTTTCGCGGCCCTTCTGCTACATGCTGGCGCTGCTGCTCA  
CTGCCGCGCTCATCTTCTTCGCCATTTGGCACATTATAGCATTTGATGAGCTGAAGACTGAT  
TACAAGAATCCTATAGACCAGTGTAATACCCTGAATCCCCTTGTA TCTCCCAGAGTACCTCAT  
CCACGCTTTCTTCTGTGTCATGTTTCTTTGTGCAGCAGAGTGGCTTACACTGGGTCTCAATA  
TGCCCCCTCTTGGCATATCATATTTGGAGGTATATGAGTAGACCAGTGATGAGTGGCCCAGGA  
CTCTATGACCCTACAACCATCATGAATGCAGATATTCTAGCATATTGTCAGAAGGAAGGATG  
GTGCAAATTAGCTTTTTATCTTCTAGCATTTTTTTACTACCTATATGGCATGATCTATGTTT  
TGGTGAGCTCTTAGAACAACACACAGAAGAATTGGTCCAGTTAAGTGCATGCAAAAAGCCAC  
CAAATGAAGGGATTCTATCCAGCAAGATCCTGTCCAAGAGTAGCCTGTGGAATCTGATCAGT  
TACTTTAAAAAATGACTCCTTATTTTTTAAATGTTTCCACATTTTTGCTTGTGGAAAGACTG  
TTTTCATATGTTATACTCAGATAAAGATTTTAAATGGTATTACGTATAAATTAATATAAAAT  
GATTACCTCTGGTGTGACAGGTTTGAACCTGCACCTCTTAAGGAACAGCCATAATCCTCTG  
AATGATGCATTAATTACTGACTGTCCTAGTACATTGGAAGCTTTTGT TATAGGAACTTGTA  
GGGCTCATTTTGGTTTCATTGAAACAGTATCTAATTATAAATTAGCTGTAGATATCAGGTGC  
TTCTGATGAAGTGAAAATGTATATCTGACTAGTGGGAACTTCATGGGTTTCCTCATCTGTC  
ATGTCGATGATTATATATGGATACATTTACAAAAATAAAAAGCGGGAATTTCCCTTCGCTT  
GAATATTATCCCTGTATATTGCATGAATGAGAGATTTCCCATATTTCCATCAGAGTAATAAA  
TATACTTGCTTTAATTCTTAAGCATAAGTAAACATGATATAAAAATATATGCTGAATTACTT  
GTGAAGAATGCATTTAAAGCTATTTTAAATGTGTTTTTATTTGTAAGACATTACTTATTAAG  
AAATTGGTTATTATGCTTACTGTTCTAATCTGGTGGTAAAGGTATTCTTAAGAATTTGCAGG  
TACTACAGATTTTCAAACTGAATGAGAGAAAATTGTATAACCATCCTGCTGTTCCCTTTAGT  
GCAATACAATAAACTCTGAAATTAAGACTC

**FIGURE 129**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA23330

<subunit 1 of 1, 144 aa, 1 stop

<MW: 16699, pI: 5.60, NX(S/T): 0

MAFTFAAFCYMLALLLTAAALIFFAIWHIIAFDELKTDYKNPIDQCNTLNPLVLPEYLIHAFF  
CVMFLCAAEWLTLGLNMPLLAYHIWRYMSRPVMSGPGLYDPTTIMNADILAYCQKEGWCKLA  
FYLLAFFYYLYGMIYVLVSS

**Important features:**

**Signal peptide:**

amino acids 1-20

**Type II transmembrane domain:**

amino acids 11-31

**Other transmembrane domain:**

amino acids 57-77 and 123-143

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**FIGURE 130**

ATTATAGCATTTGATGAGCTGAAGACTGATTACAAGATCCTATAGACCAGTGTAATACCCTG  
AATCCCCTTGTA TACTCCAGAGTACCTCATCCACGCTTTCTTCTGTGTCATGTTTCTTTGTGC  
AGCAGAGTGGCTTACACTGGGTCTCAATATGCCCCTCTTGGCATATCATATTTGGAGGTATA  
TGAGTAGACCAGTGATGAGTGGCCCAGGACTCTATGACCCTACAACCATCATGAATGCAGAT  
ATTCTAGCATATTGTCAGAAGGAAGGATGGTGCAAATTAGCTTTTTATCTTCTAGCATTTTT  
TTACTACCTATATGGCATGATCTATGTTTTGGTGAGCTCTTAGAACAACACACAGAAGAATT  
GGTCCAGTTAAGTGCATGCAAAAAGCCACCAAATGAAGGGATTCTATCCAGCAAGATCCTGT  
CCAAGAGTAGCCTGTGGAATCTGATCAGTTACTTTAAAAAATG

**FIGURE 131**

CGGACGCGTGGGGGAAACCCCTCCGAGAAAACAGCAACAAGCTGAGCTGCTGTGACAGAGGG  
GAACAAGATGGCGGCGCCGAAGGGGAGCCTCTGGGTGAGGACCCAACTGGGGCTCCCGCCGC  
TGCTGCTGCTGACCATGGCCTTGCCGGAGGTTGCGGGACCGCTTCGGCTGAAGCATTTGAC  
TCGGTCTTGGGTGATACGGCGTCTTGCCACCGGGCCTGTCAGTTGACCTACCCCTTGACAC  
CTACCCTAAGGAAGAGGAGTTGTACGCATGTCAGAGAGGTTGCAGGCTGTTTTCAATTTGTC  
AGTTTGTGGATGATGGAATTGACTTAAATCGAACTAAATTGGAATGTGAATCTGCATGTACA  
GAAGCATATTCCCAATCTGATGAGCAATATGCTTGCCATCTTGTTGCCAGAATCAGCTGCC  
ATTGCTGAACTGAGACAAGAACAATTATGTCCCTGATGCCAAAATGCACCTACTCTTTC  
CTCTAACTCTGGTGAGGTCATTCTGGAGTGACATGATGGACTCCGCACAGAGCTTCATAACC  
TCTTCATGGACTTTTTATCTTCAAGCCGATGACGGAAAAATAGTTATATTCCAGTCTAAGCC  
AGAAATCCAGTACGCACCACATTTGGAGCAGGAGCCTACAAATTTGAGAGAATCATCTCTAA  
GCAAAATGTCCTATCTGCAAATGAGAAATTCACAAGCGCACAGGAATTTCTTGAAGATGGA  
GAAAGTGATGGCTTTTTAAGATGCCTCTCTCTTAACCTCTGGGTGGATTTTAACCTACAACCTCT  
TGTCCTCTCGGTGATGGTATTGCTTTGGATTTGTTGTGCAACTGTTGCTACAGCTGTGGAGC  
AGTATGTTCCCTCTGAGAAGCTGAGTATCTATGGTGACTTGGAGTTTATGAATGAACAAAAG  
CTAAACAGATATCCAGCTTCTTCTCTTGTGGTTGTTAGATCTAAACTGAAGATCATGAAGA  
AGCAGGGCCTCTACCTACAAAAGTGAATCTTGCTCATTCTGAAATTTAAGCATTTTTCTTTT  
AAAAGACAAGTGTAATAGACATCTAAAATTCCACTCCTCATAGAGCTTTTAAAATGGTTTCA  
TTGGATATAGGCCTTAAGAAATCACTATAAAATGCAAATAAAGTTACTCAAATCTGTG

**FIGURE 132**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA26847

<subunit 1 of 1, 323 aa, 1 stop

<MW: 36223, pI: 5.06, NX(S/T): 1

MAAPKGSLLWVRTQLGLPPLLLLTMALAGGSGTASAEAFDSVLGDTASCHRAQQLTYPLHTYP  
KEEELYACQRCRLFSICQFVDDGIDLNRKLECESACTEAYSQSDEQYACHLGCONQLPFA  
ELRQEQQLMSLMPKMHLLFPLTLVRSFWSMMDSAQSFITSSWTFYLQADDGKIVIFQSKPEI  
QYAPHLEQEPTNLRESSLSKMSYLMRNSQAHRNFLEDGESDGFLRCLSLNSGWILTTTLVL  
SVMVLLWICCATVATAVEQYVPSEKLSIYGDLFMEQKLNRYPASSLVVVRSKTEDHEEAG  
PLPTKVNLAHSEI

**Important features:**

**Signal peptide:**

amino acids 1-31

**Transmembrane domain:**

amino acids 241-260

**N-glycosylation site.**

amino acids 90-93

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**FIGURE 133**

TTGGGTGATACGGCGTCTTGCCACCGGGCCTGTCAGTTGACCTACCCCTTGCACACCTACCC  
TAAGGAAGAGGAGTTGTACGCATGTCAGAGAGGTTGCAGGCTGTTTTCAATTTGTCAGTTTG  
TGGATGATGGAATTGACTTAAATCGAACTAAATTGGAATGTGAATCTGCATGTACAGAAGCA  
TATTCCCAATCTGATGAGCAATATGCTTGCCATCTTGGTTGCCAGAATCAGCTGCCATTTCGC  
TGAAGTGAGACAAGAACAACCTTATGTCCCTGATGCCAAAAATGCACCTACTCTTTCCTCTAA  
CTCTGGTGAGGTCATTCTGGAGTGACATGATGGACTCCGC

**FIGURE 134**

CACACTGGCCGGATCTTTTAGAGTCCTTTGACCTTGACCAAGGGTCNGGAAAACAGCAACAA  
GCTGAGCTGCTGTGACAGAGGGAACAAGATGGCGGCGCCGAAGGGAGCCTTTGGGTGAGGAC  
CCAAC TGGGGCTCCCGCCGCTGCTGCTGCTGACCATGGCCTTGGCCGGAGGTTCCGGGGACCG  
CTTCGGCTGAAGCATT T GACTCGGTCTTGGGTGATACGGCGTCTTGCCACCGGGCCTGTCAG  
TTGACCTACCCCTTGACACACCTACCCTAAGGAAGAGGAGTTGTACGCATGTCAGAGAGGTTG  
CAGGCTGTTTTCAATTTGTCAGTTTGTGGATGATGGAATTGACTTAAATCGAACTAAATTGG  
AATGTGAATCTGCATGTACAGAAGCATATTCCCAATCTGATGAGCAATATGCTTGCCATCTT  
GGTTGCCAGAATCAGCTGCCATTCGCTGAACTGAGACAAGAACAACCTTATGTCCCTGATGCC  
AAAAATGCACCTACTCTTTCCTCTAACTCTGGTGAGGTCATTCTGGAGTGACATGATGGACT  
CCGC

**FIGURE 135**

GCGAGGTGGCGATCGCTGAGAGGCAGGAGGGCCGAGGCGGGCCTGGGAGGCGGCCCCGGAGGT  
GGGGCGCCGCTGGGGCCGGCCCCGCACGGGCTTCATCTGAGGGCGCACGGCCCCGCGACCGAGC  
GTGCGGACTGGCCTCCCAAGCGTGGGGCGACAAGCTGCCGGAGCTGCAATGGGGCCGCGGCTG  
GGGATTCTTGTTTGGCCTCCTGGGCGCCGTGTGGCTGCTCAGCTCGGGCCACGGAGAGGAGC  
AGCCCCCGGAGACAGCGGCACAGAGGTGCTTCTGCCAGGTTAGTGGTTACTTGGATGATTGT  
ACCTGTGATGTTGAAACCATTGATAGATTTAATAACTACAGGCTTTTCCCAAGACTACAAAA  
ACTTCTTGAAAGTGACTIONTTAGGTATTACAAGGTAAACCTGAAGAGGCCGTGTCTTTCT  
GGAATGACATCAGCCAGTGTGGAAGAAGGGACTGTGCTGTCAAACCATGTCAATCTGATGAA  
GTTCTTGATGGAATTAAATCTGCGAGCTACAAGTATTCTGAAGAAGCCAATAATCTCATTGA  
AGAATGTGAACAAGCTGAACGACTTGGAGCAGTGGATGAATCTCTGAGTGAGGAAACACAGA  
AGGCTGTTCTTCAGTGGACCAAGCATGATGATTCTTCAGATAACTTCTGTGAAGCTGATGAC  
ATTCAGTCCCCTGAAGCTGAATATGTAGATTTGCTTCTTAATCCTGAGCGCTACACTGGTTA  
CAAGGGACCAGATGCTTGGAAAATATGGAATGTCATCTACGAAGAAAACCTGTTTTAAGCCAC  
AGACAATTAAAAGACCTTTAAATCCTTTGGCTTCTGGTCAAGGGACAAGTGAAGAGAACT  
TTTTACAGTTGGCTAGAAGGTCTCTGTGTAGAAAAAGAGCATTCTACAGACTTATATCTGG  
CCTACATGCAAGCATTAAATGTGCATTTGAGTGCAAGATATCTTTTACAAGAGACCTGGTTAG  
AAAAGAAATGGGGACACAACATTACAGAATTTCAACAGCGATTGATGGAATTTTGACTGAA  
GGAGAAGGTCCAAGAAGGCTTAAGAACTTGTATTTTCTCTACTTAATAGAACTAAGGGCTTT  
ATCCAAAGTGTTACCATTCTTCGAGCGCCAGATTTTCAACTCTTTACTGGAAATAAAATTC  
AGGATGAGGAAAACAAATGTTACTTCTGGAAATACTTCATGAAATCAAGTCATTTCTTTG  
CATTTTGATGAGAAATTCATTTTTTCTGGGGATAAAAAAGAGCACACAACTAAAGGAGGA  
CTTTCGACTGCATTTTAGAAATATTTCAAGAATTATGGATTGTGTTGGTTGTTTTAAATGTC  
GTCTGTGGGGAAAGCTTCAGACTCAGGGTTTGGGCACTGCTCTGAAGATCTTATTTTCTGAG  
AAATTGATAGCAAATATGCCAGAAAGTGGACCTAGTTATGAATTCATCTAACCAGACAAGA  
AATAGTATCATTATTCAACGCATTTGGAAGAATTTCTACAAGTGTGAAAGAATTAGAAACT  
TCAGGAACTTGTTACAGAATATTCATTAAAGAAAAACAAGCTGATATGTGCCTGTTTCTGGAC  
AATGGAGGCGAAAGAGTGAATTTCAATCAAAGGCATAATAGCAATGACAGTCTTAAGCCAA  
ACATTTTATATAAAGTTGCTTTTGTAAGGAGAATTATATTGTTTTAAGTAAACACATTTTT  
AAAAATTGTGTTAAGTCTATGTATAATACTACTGTGAGTAAAAGTAATACTTTAATAATGTG  
GTACAAATTTTAAAGTTAATATTGAATAAAAGGAGGATTATCAAATTAATAAAAAAAAAA  
AAAAAAAAAAAAAAAAAAAAAAAAA

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**FIGURE 136**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA53974

<subunit 1 of 1, 468 aa, 1 stop

<MW: 54393, pI: 5.63, NX(S/T): 2

MGRGWGFLFGLLGAVWLLSSSGHGEEQPPETAQRCFCQVSGYLDDCTCDVETIDRFNNYRLF  
PRLQKLLESDFRYKVNLRPCPFWNDISQCGRRDCAVKPCQSDEVDPDGIKSASYKYSEEA  
NNLIEECEQAERLGAVDESLSEETQKAVLQWTKHDDSSDNFCEADDIQSPEAEYVDLLLNPE  
RYTGKGPDAWKIWNVIYEENCFKPQTIKRPLNPLASGQGTSEENTFYSWLEGLCVEKRAFY  
RLISGLHASINVHLSARYLLQETWLEKKWGHNITEFQQRFDGILTEGEGPRRLKNLYFLYLI  
ELRALSKVLPFFERPDLFTGNKIQDEENKMLLLEILHEIKSFPLHFDENSFFAGDKKEAH  
KLKEDFRLHFRNISRIMDCVGCFCRLWGKLQTQGLGTALKILFSEKLIANMPESGPSYEFH  
LTRQEIVSLFNAFGRISTSVKELENFRNLLQNIH

**Important features:**

**Signal peptide:**

amino acids 1-23

**N-glycosylation site.**

amino acids 280-283 and 384-387

**Amidation site.**

amino acids 94-97

**Glycosaminoglycan attachment site.**

amino acids 20-23 and 223-226

**Aminotransferases class-V pyridoxal-phosphate**

amino acids 216-222

**Interleukin-7 proteins**

amino acids 338-343

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**FIGURE 137**

GCTGGAAATATGGATGTCATCTACGAGAACTGTTTTAAGCCACAGACAATTAAAAGACCTT  
TAAATCCTTTGGCTTCTGGTCAAGGGACAAGTGAAGAGNACACTTTTACAGTTGGCTAGAA  
GGTCTCTGTGTAGAAAAAAGAGCATTCTACAGACTTATATCTGGCCTACATGCAAGCATTAA  
TGTGCATTTGAGTGCAAGATATCTTTTACAAGAGACCTGGTTAGAAAAGAAATGGGGACACA  
ACATTACAGAATTTNAACAGCGATTTGATGGAATTTTGACTGAAGGAGAAGGTCCAAGAAGG  
CTTAAGAACTTGTATTTTCTCTACTTAATAGAACTAAGGGCTTTATCCAAAGTGTTACCATT  
CTTNGAGCGCCAGATTTTCAACTNTTTACTGGAAATAAAATTCAGGATGAGGNAAACAAAA  
TGTTACTTTTGGAATACTTCATGAAATCAAGTCATTTCCTTTGCATTTTGATGAGAATTCA  
TTTTTTTGCTG



**FIGURE 138**

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGTTGGGAGGGGGCAGGATGGGAGGGAA  
AGTGAAGAAAACAGAAAAGGAGAGGGACAGAGGCCAGAGGACTTCTCATACTGGACAGAAAC  
CGATCAGGCATGGAACCTCCCCTTCGTCACTCACCTGTTCTTGCCCCTGGTGTTCCTGACAGG  
TCTCTGCTCCCCCTTTAACCTGGATGAACATCACCCACGCCTATTCCCAGGGCCACCAGAAG  
CTGAATTTGGATACAGTGTCTTACAACATGTTGGGGGTGGACAGCGATGGATGCTGGTGGGC  
GCCCCCTGGGATGGGCCTTCAGGCGACCGGAGGGGGGACGTTTATCGCTGCCCTGTAGGGGG  
GGCCACAATGCCCCATGTGCCAAGGGCCACTTAGGTGACTACCAACTGGGAAATTCATCTC  
ATCCTGCTGTGAATATGCACCTGGGGATGTCTCTGTTAGAGACAGATGGTGATGGGGGATTC  
ATGGTGAGCTAAGGAGAGGGTGGTGGCAGTGTCTCTGAAGGTCCATAAAAGAAAAAGAGAA  
GTGTGGTAAGGGAAAAATGGTCTGTGTGGAGGGGTCAAGGAGTTAAAAACCTAGAAAGCAAA  
AGGTAGGTAATGTCAGGGAGTAGTCTTCATGCCTCCTTCAACTGGGAGCATGTTCTGAGGGT  
GCCCTCCCAAGCCTGGGAGTAACCTATTTCCCCCATCCCCAGGCCTGTGCCCCCTCTCTGGTCT  
CGTGCTTGTGGCAGCTCTGTCTTCAGTTCTGGGATATGTGCCCCGTGTGGATGCTTCATTCCA  
GCCTCAGGGAAGCCTGGCACCCACTGCCAACGTGAGCCAGAGGAAGGCTGAGTACTTGGTT  
CCCAGAAGGAGATACTGGGTGGGAAAAAGATGGGGCAAAGCGGTATGATGCCTGGCAAAGGG  
CCTGCATGGCTATCCTCATTGCTACCTAATGTGCTTGCAAAGCTCCATGTTTCCTAACAGA  
TTCAGACTCCTGGCCAGGTGTGGTGGCCACACCTGTAATTCTAGCACTTTGGGAGGCCAAG  
GTGGGCAGATCACTTGAGGTGAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACTCCAT  
CTCTACTAAAAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAAATAA  
ATCTACTCGGGAGGCTAAGACAGGAGACTCTCACTTCAACCCAGGAGGTGGAGGTTGCGGTG  
AGCCAAGATTGTGCCTCTGCACTCTAGCGTGGGTGACAGAGTAAGCGAGACTCCATCTCAAA  
AATAATAATAATAATAATTCAGACTCCTTATCAGGAGTCCATGATCTGGCCTGGCACAGTAA  
CTCATGCCTGTAATCCCAACATTTTGGGAGGCCAACGCAGGAGGATTGCTTGAGGTCTGGAG  
GTTTGAGACCAGCCTGGGCAACATAGAAAGACCCCATCTCTAAATAAATGTTTTAAAAAT

**FIGURE 139**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA57039

><subunit 1 of 1, 124 aa, 1 stop

><MW: 13352, pI: 5.99, NX(S/T): 1

MELPFVTHLFLPLVFLTGLCSPFNLDEHHPRLFPGPPEAEFGYSVLQHVGGGQRWMLVGAPW  
DGPSGDRRGDVYRCPVGGAHNAPCAKGHLGDYQLGNSSHPAVNMHLGMSLLETGDGGMVS

**Important features:**

**Signal peptide:**

amino acids 1-22

**Cell attachment sequence.**

amino acids 70-73

**N-glycosylation site.**

amino acids 98-101

**Integrins alpha chain proteins**

amino acids 67-81

**FIGURE 140**

CACAGTTCCCCACCATCACTCNTCCCATTCCTTCCAACCTTTATTTTGTAGCTTGCCATTGGGA  
GGGGGCAGGATGGGAGGGAAAGTGAAGAAAACAGAAAAGGAGAGGGACAGAGGCCAGAGGAC  
TTCTCATACTGGACAGAAACCGATCAGGCATGGAACCTCCCCTTCGTCACCTGTTCTTG  
CCCCTGGTGTTCTTGACAGGTCTCTGCTCCCCCTTTAACCTGGATGAACATCACCCACGCCT  
ATTTCCAGGGCCACCAGAAGCTGAATTTGGATACAGTGTCTTACAACATGTTGGGGGTGGAC  
AGCGATGGATGCTGGTGGGCGCCCCCTGGGATGGGCCTTCAGGCGACCGGAGGGGGGACGTT  
TATCGCTGCCCTGTAGGGGGGGCCACAATGCCCCATGTGCCAAGGGCCACTTAGGTGACTA  
CCAAGTGGGAAATTCATCTCATCCTGCTGTGAATATGCACCTGGGGATGTCTCTGTAGAGA  
CAGATGGTGATGG

**FIGURE 141**

AAAGTTACATTTTCTCTGGAACCTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG  
GGCAGAAAGGAGGGTGCTTCGGAGCCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAACA  
ATTGAGGCTTCGCTGCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCT  
GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACCTGAGTCTACCA  
AATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTTCT  
ACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGCCTGCCCCCTCAGAACCTC  
TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA  
AACAGTGTACTATTCTGTGCAATACCAGGGGGGAGTACGAGAGCCTGTACACGAGCCACATCT  
GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCTGAGTGTGATGTCACTGATGACATC  
ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG  
GAGCATCCTGAAGCATCCCTTTAATAGAACTCAACCATCCTTACCCGACCTGGGATGGAGA  
TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC  
CTTGTTGGCCTACTGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGG  
GGGTATTCAGTGCACCTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA  
CATTGTTGAAGGCCATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAA  
GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCCCTTTGTTGGCTTCATGCTGATCCTTGT  
GGTCGTGCCACTGTTTCGTCTGGAAAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCCGTGG  
TGGTCCTCCCAGACACCTTGAAAATAACCAATTACCCCCAGAAGTTAATCAGCTGCAGAAGG  
GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCTGAGGAACTCCTCAGGGCCTGGAT  
CTCATAGGTTTTCGGAAGGGGCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC  
ATGAGGGGACAAGTTGTGTTTCTGTTTTCCGCCACGGACAAGGGATGAGAGAAGTAGGAAGA  
GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC  
TGACTGAGGCTTAGGGGATGTGACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACC  
CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC  
TACACACCTGCTAAACACACACACAGAGTCTCTCTATATATACACACGTACACATAAA  
TACACCAGCACTTGCAAGGCTAGAGGGAACTGGTGACACTCTACAGTCTGACTGATTGAG  
TGTTTCTGGAGAGCAGGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT  
GGCTTGAGAGCCCACTTTCCCGAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG  
TGTTGAGTTCACTTCAAGCCCAATGCCGGTGACAGGGGAATGGCTTAGCGAGCTCTACAGT  
AGGTGACCTGGAGGAAGGTCACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC  
CATGAACTACTGTAAAGTGTGACAGTGTGTGCACACTGCAGACAGCAGGTGAAATGTATGT  
GTGCAATGCGACGAGAATGCAGAAGTCAGTAACATGTGCATGTTTGTGTGCTCCTTTTTTC  
TGTTGGTAAAGTACAGAATTCAGCAAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAAA  
AAAAAAAAA

**FIGURE 142**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA57033

<subunit 1 of 1, 311 aa, 1 stop

<MW: 35076, pI: 5.04, NX(S/T): 2

MQTFMTVLEEIWTSLEFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHLIMWSPVIAPGE  
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDVTDDITATVPYNLRVRATLGSQTS  
SAW  
SILKHPFNRNSTILTRPGMEITKDGFHLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSG  
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPVLALFAFVGFMILIV  
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

**Important features:**

**Signal peptide:**

amino acids 1-29

**Transmembrane domain:**

amino acids 230-255

**N-glycosylation site.**

amino acids 40-43 and 134-137

**Tissue factor proteins.**

amino acids 92-119

**Integrins alpha chain proteins**

amino acids 232-262

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**FIGURE 143**

TCCTGCTGATGCACATCTGGGTTTGGCAAAGGAGGTTGCTTCGAGCCGCCCTTTCTAGCTT  
CCTGGCCGGCTCTAGAACAATTCAGGCTTCGCTGCGACTAGACCTCAGCTCCAACATATGCA  
TTCTGAAGAAAGATGGCTGAGATGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGG  
TCAAACCTGAGTCTACCAAATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCT  
TTTCATGTGGTTTTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC  
CTGCCCCCTCAGAACCTCTCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCA  
GTGATCGCGCCTGGAGAAACAGTGTACTATTCTGTGCGAATACCAGGGGGAGTACGAGAGCCT  
GTACACGAGCCACATCTGGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTG  
ATGTCACTGATGACATCACGGCCACTGTGCCATACAACCTTTGTGTCAGGGCCACATTGGGC  
TCACAGACCTCAGCCTGGAGCATCCTGAAGCATCCCTTTAATAGAACTCAACCATCCTTAC  
CCGACCTGGGATGGAGATCACCAAAGATGGCTTNCACCTGGTTATTGAGCTGGAGGACCTGG  
GGCCCCAGTTTGAGTTCCTTGTGGCCTANTGGAGGAGGGGCGAACCCCTTGCGGCGCAAGGG  
GTTNGCGAACCCCTTGCGGCCGCTGGGGTATCTCTCGAGAAAAGAGAGGCCCAATATGACCC  
ACATACTCAATATGGACGAANTGCTATTGTCCACCTGTTTGAGTGGCGCTGGGTTGAT

**FIGURE 144**

CCCACGCGTCCGCCCACGCGTCCGAGGGACAAGAGAGAAGAGAGACTGAAACAGGGAGAAGA  
GGCAGGAGAGGAGGAGGTGGGGAGAGCACGAAGCTGGAGGCCGACACTGAGGGAGGGCGGGA  
GGAGGTGAAGAAGGAGAGAGAGGGGAGAAGAGGCAGGAGCTGGAAAGGAGAGAGGGAGGAGGAG  
GAGGAGATGCGGGATGGAGACCTGGAGTTAGGTGGCTTGGGAGAGCTTAATGAAAAGAGAAC  
GGAGAGGAGGTGTGGGTTAGGAACCAAGAGGTAGCCCTGTGGGCAGCAGAAGGCTGAGAGGA  
GTAGGAAGATCAGGAGCTAGAGGGAGACTGGAGGGTTCCGGGAAAAGAGCAGAGGAAAGAGG  
AAAGACACAGAGAGACGGGAGAGAGAAGAAGAGTGGGTTTGAAGGGCGGATCTCAGTCCCTG  
GCTGCTTTGGCATTGTTGGGAACTGGGACTCCCTGTGGGGAGGAGAGGAAAGCTGGAAGTCCT  
GGAGGGACAGGGTCCCAGAAGGAGGGGACAGAGGAGCTGAGAGAGGGGGGACAGGGCGTTGGG  
CAGGGGTCCCTCGGAGGCCTCCTGGGGATGGGGCTGCAGCTCGTCTGAGCGCCCCCTCGAGC  
GCTGGTACTCTGGGCTGCACTGGGGGCAGCAGCTCACATCGGACCAGCACCTGACCCCGAGG  
ACTGGTGGAGCTACAAGGATAATCTCCAGGGAACTTCGTGCCAGGGCCTCCTTTCTGGGGC  
CTGGTGAATGCAGCGTGGAGTCTGTGTGCTGTGGGGAAGCGGCAGAGCCCCGTGGATGTGGA  
GCTGAAGAGGGTTCTTTATGACCCCTTTCTGCCCCATTAAGGCTCAGCACTGGAGGAGAGA  
AGCTCCGGGGAACCTTGTACAACACCGGCCGACATGTCTCCTTCCTGCCTGCACCCCGACCT  
GTGGTCAATGTGTCTGGAGGTCCCTCCTTTACAGCCACCGACTCAGTGAAGTGCGGCTGCT  
GTTTGGAGCTCGCGACGGAGCCGGCTCGGAACATCAGATCAACCACCAGGGCTTCTCTGCTG  
AGGTGCAGCTCATTCACTTCAACCAGGAACTCTACGGGAATTTAGCGCTGCCTCCCGCGGC  
CCCAATGGCCTGGCCATTCTCAGCCTCTTTGTCAACGTTGCCAGTACCTCTAACCATTCTC  
CAGTCGCCTCCTTAACCGCGACACCATCACTCGCATCTECTACAAGAATGATGCCTACTTTC  
TTCAAGACCTGAGCCTGGAGCTCCTGTTCCCTGAATCCTTCGGCTTCATCACCTATCAGGGC  
TCTCTCAGCACCCCGCCCTGCTCCGAGACTGTCACCTGGATCCTCATTGACCGGGCCCTCAA  
TATCACCTCCCTTCAGATGCACTCCCTGAGACTCCTGAGCCAGAATCCTCCATCTCAGATCT  
TCCAGAGCCTCAGCGGTAACAGCCGGCCCCCTGCAGCCCTTGGCCACAGGGCACTGAGGGGC  
AACAGGGACCCCGGCACCCCGAGAGGCGCTGCCGAGGCCCCAACTACCGCCTGCATGTGGA  
TGGTGTCCCCCATGGTCGCTGAGACTCCCCCTCGAGGATTGCACCCGCGCGTCTTAAGCCTC  
CCCACAAGGCGAGGGGAGTTACCCCTAAAACAAAGCTATTAAAGGGACAGAATACTTA

**FIGURE 145**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA34353

<subunit 1 of 1, 328 aa, 1 stop

<MW: 36238, pI: 9.90, NX(S/T): 3

MGAAARLSAPRALVLWAALGAAAHIGPAPDPEDWWSYKDNLQGNFVPGPPFWGLVNAAWSLC  
AVGKRQSPVDVELKRVLYDPFLPPLRLSTGGEKLRGTLTYNTGRHVSFLPAPRPVVNVSGGPL  
LYSHRLSELRLLFGLRDGAGSEHQINHQGFSAEVQLIHFNQELYGNFSAASRGPNGLAILSL  
FVNVASTSNPFLSRLLRDITRISYKNDAYFLQDLSLELLFPESFGFITYQGSLSLTPPCSE  
TVTWILIDRALNITSLQMHSLRLLSQNPSPQIFQSLSGNSRPLQPLAHRALRGNRDPRHPER  
RCRGPNYRLHVDGVPHGR

**Important features:**

**Signal peptide:**

amino acids 1-23

**Transmembrane domain:**

amino acids 177-199

**N-glycosylation site.**

amino acids 118-121, 170-173 and 260-263

**Eukaryotic-type carbonic anhydrases proteins**

amino acids 222-270, 128-164 and 45-92



**FIGURE 146**

GGCGCCTGGTCTGCGCGTACTGGCTGTACGGAGCAGGAGCAAGAGGTGCGCGCCAGCCTCC  
GCCGCCGAGCCTCGTTCGTGTCCCCGCCCTCGCTCCTGCAGCTACTGCTCAGAAACGCTGG  
GGCGCCCACCCTGGCAGACTAACGAAGCAGCTCCCTTCCCACCCCAACTGCAGGTCTAATTT  
TGGACGCTTTGCCTGCCATTTCTTCCAGGTTGAGGGAGCCGCAGAGGCGGAGGCTCGCGTAT  
TCCTGCAGTCAGCACCCACGTCGCCCCCGACGCTCGGTGCTCAGGCCCTTCGCGAGCGGGG  
CTCTCCGTCTGCGGTCCCTTGTGAAGGCTCTGGGCGGCTGCAGAGGCCGCGCGTCCGGTTTG  
GCTCACCTCTCCCAGGAACTTCACACTGGAGAGCCAAAAGGAGTGGAAGAGCCTGTCTTGG  
AGATTTTCTGGGGAAATCCTGAGGTCATTATTATGAAGTGTACCGCGCGGGAGTGGCTCA  
GAGTAACCACAGTGCTGTTTCATGGCTAGAGCAATTCAGCCATGGTGGTTCCCAATGCCACT  
TTATTGGAGAACTTTTGGAAAAATACATGGATGAGGATGGTGAGTGGTGGATAGCCAAACA  
ACGAGGGGAAAAGGGCCATCACAGACAATGACATGCAGAGTATTTTGGACCTTCATAATAAAT  
TACGAAGTCAGGTGTATCCAACAGCCTTAATATGGAGTATATGACATGGGATGTAGAGCTG  
GAAAGATCTGCAGAATCCTGGGCTGAAAGTTGCTTGTGGGAACATGGACCTGCAAGCTTGCT  
TCCATCAATTGGACAGAATTTGGGAGCACACTGGGGAAGATATAGGCCCCGACGTTTCATG  
TACAATCGTGGTATGATGAAGTGAAAGACTTTAGCTACCCATATGAACATGAATGCAACCCA  
TATTGTCCATTTCAGGTGTTCTGGCCCTGTATGTACACATTATACACAGGTCGTGTGGGCAAC  
TAGTAACAGAATCGGTTGTGCCATTAATTTGTGTACATAACATGAACATCTGGGGGCAGATAT  
GGCCCAAAGCTGTCTACCTGGTGTGCAATTACTCCCCAAAGGGAACTGGTGGGGCCATGCC  
CCTTACAAACATGGGCGGCCCTGTTCTGCTTGGCCACCTAGTTTTGGAGGGGGCTGTAGAGA  
AAATCTGTGCTACAAAGAAGGGTCAGACAGGTATTATCCCCCTCGAGAAGAGGAAACAAATG  
AAATAGAACGACAGCAGTCACAAGTCCATGACACCCATGTCCGGACAAGATCAGATGATAGT  
AGCAGAAATGAAGTCATAAGCGCACAGCAAATGTCCCAAATTGTTTCTTGTGAAGTAAGATT  
AAGAGATCAGTGCAAAGGAACAACCTGCAATAGGTACGAATGTCTGCTGGCTGTTTGGATA  
GTAAAGCTAAAGTTATTGGCAGTGTACATTATGAAATGCAATCCAGCATCTGTAGAGCTGCA  
ATTCAATTATGGTATAATAGACAATGATGGTGGCTGGGTAGATATCACTAGACAAGGAAGAAA  
GCATTATTTTCATCAAGTCCAATAGAAATGGTATTCAAACAATTGGCAAATATCAGTCTGCTA  
ATTCTTCACAGTCTCTAAAGTAACAGTTCAGGCTGTGACTTGTGAAACAACCTGTGGAACAG  
CTCTGTCCATTTTCATAAGCCTGCTTCACATTGCCCAAGAGTATACTGTCTCGTAACTGTAT  
GCAAGCAAATCCACATTATGCTCGTGTAAATTGGAACCTCGAGTTTATTCTGATCTGTCCAGTA  
TCTGCAGAGCAGCAGTACATGCTGGAGTGGTTCGAAATCACGGTGGTTATGTTGATGTAATG  
CCTGTGGACAAAAGAAAGACCTACATTGCTTCTTTTCAGAATGGAATCTTCTCAGAAAGTTT  
ACAGAATCCTCCAGGAGGAAAGGCATTTCAGAGTGTGTTGCTGTTGTGTGAAACTGAATACTTG  
GAAGAGGACCATAAAGACTATTCCAAATGCAATATTTCTGAATTTTGTATAAAACTGTAACA  
TTACTGTACAGAGTACATCAACTATTTTCAGCCCCAAAAGGTGCCAAATGCATATAAATCTT  
GATAAACAAAGTCTATAAAATAAAACATGGGACATTAGCTTTGGGAAAAGTAATGAAAATAT  
AATGGTTTTAGAAATCCTGTGTAAATATTGCTATATTTTCTTAGCAGTTATTTCTACAGTT  
AATTACATAGTCATGATTGTTCTACGTTTCATATATTATATGGTGGCTTGTATATGCCACTA  
ATAAAATGAATCTAAACATTGAATGTGAATGGCCCTCAGAAAATCATCTAGTGCATTTAAAA  
ATAATCGACTCTAAAACCTGAAAGAAACCTTATCACATTTCCCCAGTTCATGCTATGCCAT  
TACCAACTCCAAATAATCTCAAATAATTTCCACTTAATAACTGTAAAGTTTTTTTCTGTTA  
ATTTAGGCATATAGAATATTAAATTCTGATATTGCACCTCTTATTTTATATAAAATAATCCT  
TTAATATCCAAATGAATCTGTAAATGTTTGATTCTTGGGAATGGCCTTAAAAATAAATG  
TAATAAAGTCAGAGTGGTGGTATGAAAACATTCTAGTGATCATGTAGTAAATGTAGGGTTA  
AGCATGGACAGCCAGAGCTTCTATGTACTGTTAAAATTGAGGTACATATTTTCTTTTGTA  
TCCTGGCAAATACTCCTGCAGGCCAGGAAGTATAATAGCAAAAAGTTGAACAAAGATGAAC  
AATGTATTACATTACCATTGCCACTGATTTTTTTTTTAAATGGTAAATGACCTTGTATATAAAT  
ATTGCCATATCATGGTACCTATAATGGTGATATATTTGTTTCTATGAAAAATGTATTGTGCT  
TTGATACTAAAAATCTGTAAATGTTAGTTTTTGGTAATTTTTTTTCTGCTGGTGGATTTACA  
TATTAAATTTTTTCTGCTGGTGGATAAACATTAAATTAATCATGTTTCAAAAAAAAAAAAA

**FIGURE 147**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45417

<subunit 1 of 1, 500 aa, 1 stop

<MW: 56888, pI: 8.53, NX(S/T): 2

MKCTAREWLRVTTVLFMARAI PAMVVPNATLLEKLLEKYMDEDEGEWWIAKQRGKRAITDNDM  
QSILDLHNKLR SQVYPTASNMEYMTWDVELERSAESWAESCLWEHGPASLLPSIGQNLGAHW  
GRYRPPTFHVQSWYDEVKDFSYPEHECNPYCPFRCSGPVCTHYTQV VWATSNRIGCAINLC  
HNMNIWGQIWPKAVYLV CNYSPKGNWWGHAPYKHGRPCSACPPSFGGGCRENLCYKEGSDRY  
YPPREEETNEIERQQSQVHDTHVTRTRSDSSRNEVIS AQMSQIVSCEVRLRDQCKGTTTCNR  
YEC PAGCLDSKAKVIGSVHYEMQSSICRAAIHYGIIDNDGGWVDITRQGRKH YFIKSNRNGI  
QTIGKYQSANSFTVSKVTVQAVTCETTVEQLCPFHKPASHCPRVYCP RNCMQANPHYARVIG  
TRVYSDLSSICRAAVHAGVVRNHGGYVDMPVDKRKTYIASFQNGIFSES LQNPPGGKA FRV  
FAVV

**Important features:**

**Signal peptide:**

amino acids 1-20

**Extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 protein**

amino acids 165-186, 196-218, 134-146, 96-108 and 58-77

**N-glycosylation site**

amino acids 28-31

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**FIGURE 148**

GCGGAGACAAGCGCAGAGCGCAGCGCACGGCCACAGACAGCCCTGGGCATCCACCGACGGCG  
CAGCCGGAGCCAGCAGAGCCGGAAGGCGCGCCCCGGGCAGAGAAAGCCGAGCAGAGCTGGGT  
GGCGTCTCCGGGCCGCCGCTCCGACGGGCCAGCGCCCTCCCCATGTCCCTGCTCCACGCCG  
CGCCCCCTCCGGTCAGCATGAGGCTCCTGGCGGCCGCGCTGCTCCTGCTGCTGCTGGCGCTGT  
ACACCGCGCGTGTGGACGGGTCCAAATGCAAGTGCTCCCGGAAGGGACCCAAGATCCGCTAC  
AGCGACGTGAAGAAGCTGGAAATGAAGCCAAAGTACCCGCACTGCGAGGAGAAGATGGTTAT  
CATCACCACCAAGAGCGTGTCCAGGTACCGAGGTCAGGAGCACTGCCTGCACCCCAAGCTGC  
AGAGCACCAAGCGCTTCATCAAGTGGTACAACGCCTGGAACGAGAAGCGCAGGGTCTACGAA  
GAATAGGGTGAAAAACCTCAGAAGGGAAAACTCCAAACCAGTTGGGAGACTTGTGCAAAGGA  
CTTTGCAGATTAAAAAAGCCTTTT  
TTTCTCACAGGCATAAGACACAAATTATATATTGTTATGAAGCACTTTTTACCAACGGTCAG  
TTTTTACATTTTATAGCTGCGTGCGAAAGGCTTCAGATGGGAGACCCATCTCTCTTGTGCT  
CCAGACTTCATCACAGGCTGCTTTTTATCAAAAAGGGGAAAACTCATGCCTTTCCTTTTTAA  
AAAATGCTTTTTTGTATTTGTCCATACGTCACTATACATCTGAGCTTTATAAGCGCCCGGA  
GGAACAATGAGCTTGGTGGACACATTTTCATTGCAGTGTTGCTCCATTCTAGCTTGGGAAGC  
TTCCGCTTAGAGGTCTGGCGCCTCGGCACAGCTGCCACGGGCTCTCCTGGGCTTATGGCCG  
GTCACAGCCTCAGTGCTGACTCCACAGTGGCCCCCTGTAGCCGGGCAAGCAGGAGCAGGTCTCT  
CTGCATCTGTTCTCTGAGGAACTCAAGTTTGGTTGCCAGAAAAATGTGCTTCATCCCCCCT  
GGTTAATTTTACACACCCTAGGAAACATTTCCAAGATCCTGTGATGCCGAGACAAATGATC  
CTTAAAGAAGGTGTGGGGTCTTTCCCAACCTGAGGATTTCTGAAAGGTTACAGGTTCAATA  
TTTAATGCTTCAGAAGCATGTGAGGTTCCCAACACTGTCAGCAAAAACCTTAGGAGAAAACT  
TAAAAATATATGAATACATGCGCAATACACAGCTACAGACACACATTCTGTTGACAAGGGAA  
AACCTTCAAAGCATGTTTCTTTCCCTCACCACAACAGAACATGCAGTACTAAAGCAATATAT  
TTGTGATTCCCATGTAATTCTTCAATGTTAAACAGTGCAGTCCTCTTTCGAAAGCTAAGAT  
GACCATGCGCCCTTTCCTCTGTACATATACCCTTAAGAACGCCCCCTCCACACACTGCCCC  
CAGTATATGCCGCATTGTACTGCTGTGTTATATGCTATGTACATGTCAGAAACCATTAGCAT  
TGCATGCAGGTTTCATATTCTTTCTAAGATGGAAAGTAATAAAATATATTTGAAATGTAAAA  
AAAAAAAAAA

## FIGURE 149

MSLLPRRAPVSMRLLAAALLLLLLALYTARVDGSKCKCSRKGPKIRYSDVKKLEMKPKYPH  
CEEKMWIITTKSVSRYRGQEHCLHPKLQSTKRFIKWYNWNEKRRVYEE

**FIGURE 150**

GCCCCAGGGACTGCTATGGCTTCCTTTGTTGTTACCCCGGTCTGCGTCAATGTTAAACTCCA  
ATGTCTCTCTGTGGTTAACTGCTCTTGCCATCAAGTTCACCCCTATTGACAGCCAAGCACAG  
TATCCAGTTGTCAACACAAATTATGGCAAATCCGGGGCCTAAGAACACCGTTACCCAATGA  
GATCTTGGGTCCAGTGGAGCAGTACTTAGGGGTCCCCTATGCCTCACCCCCCACTGGAGAGA  
GGCGGTTTCAGCCCCCAGAACCCCCGTCTCTGGACTGGCATCCGAAATACTACTCAGTTT  
GCTGCTGTGTGCCCCCAGCACCTGGATGAGAGATCCTTACTGCATGACATGCTGCCCATCTG  
GTTTACCGCCAATTTGGATACTTTGATGACCTATGTTCAAGATCAAAATGAAGACTGCCTTT  
ACTTAAACATCTACGTGCCCACGGAAGATGGAGCCAACACAAAGAAAAACGCAGATGATATA  
ACGAGTAATGACCGTGGTGAAGACGAAGATATTATCATGATCAGAACAGTAAGAAGCCCGTCAT  
GGTCTATATCCATGGGGGATCTTACATGGAGGGCACC GGCAACATGATTGACGGCAGCATT  
TGGCAAGCTACGGAAACGTATCGTGATCACCATTAACTACCGTCTGGGAATACTAGGGTTT  
TTAAGTACCGGTGACCAGGCAGCAAAAGGCAACTATGGGCTCCTGGATCAGATTCAAGCACT  
GCGGTGGATTGAGGAGAATGTGGGAGCCTTTGGCGGGGACCCCAAGAGAGTGACCATCTTTG  
GCTCGGGGGCTGGGGCCTCCTGTGTGTCAGCCTGTTGACCCTGTCCCACTACTCAGAAGGTCTC  
TTCCAGAAGGCCATCATTAGAGCGGCACCGCCCTGTCCAGCTGGGCAGTGAAGTACCAGCC  
GGCCAAGTACACTCGGATATTGGCAGACAAGGTCGGCTGCAACATGCTGGACACCACGGACA  
TGGTAGAATGCCTGCGGAACAAGAACTACAAGGAGCTCATCCAGCAGACCATCACCCCGGCC  
ACCTACCACATAGCCTTCGGGCCGGTGATCGACGGCGACGTATCCAGACGACCCCCAGAT  
CCTGATGGAGCAAGGCGAGTTCTCAACTACGACATCATGCTGGGCGTCAACCAAGGGGAAG  
GCCTGAAGTTTCGTGGACGGCATCGTGATAACGAGGACGGTGTGACGCCCCAACGACTTTGAC  
TTCTCCGTGTCCAACCTTCGTGGACAACCTTTACGGCTACCCTGAAGGGAAAGACACTTTGCG  
GGAGACTATCAAGTTCATGTACACAGACTGGGCGGATAAGGAAAACCCGGAGACGCGGCGGA  
AAACCCTGGTGGCTCTCTTTACTGACCACCAGTGGGTGGCCCCCGCGGTGGCCCGGACCTG  
CACGCGCAGTACGGCTCCCCACCTACTTCTATGCCTTCTATCATCACTGCCAAAGCGAAAT  
GAAGCCCAGCTGGGCAGATTTCGGCCCATGGTGATGAGGTCCCCTATGTCTTCGGCATCCCCA  
TGATCGGTCCCACCGAGCTCTCAGTTGTAACCTTTTCCAAGAACGACGTACATGCTCAGCGCC  
GTGGTCATGACCTACTGGACGAACTTCGCCAAAACCTGGTGATCCAAATCAACCAGTTCTCTCA  
GGATACCAAGTTCATTCACACAAAACCCAACCGCTTTGAAGAAGTGGCCTGGTCCAAGTATA  
ATCCCAAAGACCAGCTCTATCTGCATATTGGCTTGAAACCCAGAGTGAGAGATCACTACCGG  
GCAACGAAAGTGGCTTTCTGGTTGGAACCTCGTTCCTCATTGACAACTTGAACGAGATATT  
CCAGTATGTTTCAACAACCACAAAGGTTCTCTCCACCAGACATGACATCATTTCCTATGGCA  
CCCGGCGATCTCCCGCCAAGATATGGCCAACCACCAACGCCAGCAATCACTCCTGCCAAC  
AATCCCAAACACTCTAAGGACCCTCACAAAACAGGGCCTGAGGACACAACCTGTCTCATTGA  
AACCAAACGAGATTATTCCACCGAATTAAGTGTCACCATTGCCGTGCGGGCGTCTCTCTCT  
TCCTCAACATCTTAGCTTTTGGCGGCTGTACTACAAAAGGACAAGAGGCGCCATGAGACT  
CACAGGCGCCCCAGTCCCCAGAGAAACACCACAAATGATATCGCTCACATCCAGAACGAAGA  
GATCATGTCTCTGCAGATGAAGCAGCTGGAACACGATCACGAGTGTGAGTCGCTGCAGGCAC  
ACGACACACTGAGGCTCACCTGCCCGCCAGACTACACCCTCACGCTGCGCCGGTCCGCAGAT  
GACATCCCCTTATGACGCCAAACACCATCACCATGATTCCAAACACACTGACGGGGATGCA  
GCCTTTGCACACTTTTAAACACCTTCAGTGGAGGACAAAACAGTACAAATTTACCCACGGAC  
ATTCCACCACTAGAGTATAGCTTTGCCCTATTTCCCTTCTATCCCTCTGCCCTACCCGCTC  
AGCAACATAGAAGAGGGAAGGAAAGAGAGAAGGAAAGAGAGAGAGAAAGAAAGTCTCCAGAC  
CAGGAATGTTTTTGTCCCACTGACTTAAGACAAAATGCAAAAAGGCAGTCATCCCATCCCG  
GCAGACCCTTATCGTTGGTGTTTTCCAGTATTACAAGATCAACTTCTGACCCTGTGAAATGT  
GAGAAGTACACATTTCTGTAAATAACTGCTTTAAGATCTCTACCACTCCAATCAATGTTT  
AGTGTGATAGGACATCACCATTTCAGGGCCCCGGGTGTTTCCAACGTCATGGAAGCAGCTGA  
CACTTCTGAAACTCAGCCAAGGACACTTGATATTTTAAATTACAATGGAAGTTTAAACATT  
TCTTTCTGTGCCACACAATGGATGGCTCTCCTTAAGTGAAGAAAGAGTCAATGAGATTTTGC  
CCAGCACATGGAGCTGTAATCCAGAGAGAAGGAAACGTAGAAATTTATTATTAAAGAATGG  
ACTGTGCAGCGAAATCTGTACGGTTCTGTGCAAGAGGTGTTTGGCAGCCTGAAGTATATT  
TAAGAGACTTTGT

**FIGURE 151**

MLNSNVLLWLTALAIKFTLIDSQAQYPVVNTNYGKIRGLRTPLPNEILGPVEQYLGVPYASP  
PTGERRFQPPEPPSSWTGIRNTTQFAAVCPQHLDERSLLHDMLEPIWFTANLDTLMTYVQDON  
EDCLYLNIYVPTEDGANTKKNADDITSNDRGEDEDIHDQNSKKPVMVYIHGGSYMEGTGNMI  
DGSILASYGNVIVITINYRLGILGFLSTGDQAAKGNYGLLDQIQALRWIEENVGAFFGGDPKR  
VTIFGSGAGASCVSLLTLSHYSEGLFQKAI IQSGTALSSWAVNYQPAKYTRILADKVGCMML  
DTTDMVECLRNKNYKELIQQTITPATYHIAFGPVIDGDVIPDDPQILMEQGEFLNYDIMLGV  
NQGEGLKFVDGIVDNEDGVTPNDFDFSVSNFVDNLYGYPEGKDTLRETIKMYTDWADKENP  
ETRRKTLVALFTDHQWVAPAVAADLHAQYGSPTYFYAFYHHCQSEMKPSWADSAGHDEVYV  
FGIPMIGPTELFSCNFSKNDVMLS AVVMTYWTNFAKTGDPNQVPQDTKFIHTKPNRFEEVA  
WSKYNPKDQLYLHIGLKPRVRDHYRATKVAFWLELVPHLHNLNEIFQYVSTTTKVPPPDMS  
FPYGTRRSPAKIWPTTKRPAITPANNPKHSDPHKTGPEDTTVLIETKRDYSTEISVTI AVG  
ASLLFLNILAFAALYYKKDKRRHETHRRPSPQRNTTNDIAHIQNEEIMSLQMKQLEHDHECE  
SLQAHDTLRLTCPPDYTLTLRRSPDDIPLMTPNTITMIPNTLTGMQPLHTFNTFSGGQNSTN  
LPHGHSTTRV

**FIGURE 152**

GGGAAAGATGGCGGCGACTCTGGGACCCCTTGGGTCTGGCAGCAGTGGCGGCGATGTTTGT  
CGGCTCGGGATGGGTCCAGGATGTTACTCCTTCTTCTTTGTTGGGGTCTGGGCAGGGGCCA  
CAGCAAGTCGGGGCGGGTCAAACGTTTCGAGTACTTGAAACGGGAGCACTCGCTGTGAAGCC  
CTACCAGGGTGTGGGCACAGGCAGTTCCTCACTGTGGAATCTGATGGGCAATGCCATGGTGA  
TGACCCAGTATATCCGCCTTACCCAGATATGCAAAGTAAACAGGGTGCCTTGTGGAACCGG  
GTGCCATGTTTCTGAGAGACTGGGAGTTGCAGGTGCACTTCAAATCCATGGACAAGGAAA  
GAAGAATCTGCATGGGGATGGCTTGGCAATCTGGTACACAAAGGATCGGATGCAGCCAGGGC  
CTGTGTTTGGAAACATGGACAAATTTGTGGGGCTGGGAGTATTTGTAGACACCTACCCCAAT  
GAGGAGAAGCAGCAAGAGCGGGTATTCCCTACATCTCAGCCATGGTGAACAACGGCTCCCT  
CAGCTATGATCATGAGCGGGATGGGCGGCCTACAGAGCTGGGAGGCTGCACAGCCATTGTCC  
GCAATCTTCATTACGACACCTTCCTGGTGAATTCGCTACGTCAAGAGGCATTTGACGATAATG  
ATGGATATTGATGGCAAGCATGAGTGGAGGGACTGCATTGAAGTGCCCGGAGTCCGCCTGCC  
CCGCGGCTACTACTTCGGCACCTCCTCCATCACTGGGGATCTCTCAGATAATCATGATGTCA  
TTTCTTGAAGTTGTTTGAAGTACAGTGGAGAGAACCCAGAAAGAGGAAAAGCTCCATCGA  
GATGTGTTCTTGCCCTCAGTGGACAATATGAAGCTGCCTGAGATGACAGCTCCACTGCCGCC  
CCTGAGTGGCCTGGCCCTCTTCTCATCGTCTTTTCTCCCTGGTGTCTTCTGTATTTGCCA  
TAGTCATTGGTATCATACTCTACAACAAATGGCAGGAACAGAGCCGAAAGCGCTTCTACTGA  
GCCCTCCTGCTGCCACCCTTTTGTGACTGTCAACCATGAGGTATGGAAGGAGCAGGCAGT  
GCCTGAGCATGCAGCCTGGAGAGTGTCTTGTCTCTAGCAGCTGGTTGGGGACTATATTCTG  
TCACTGGAGTTTTGAATGCAGGGACCCCGCAATCCCATGGTTGTGCATGGGGACATCTAACT  
CTGGTCTGGGAAGCCACCCACCCAGGGCAATGCTGCTGTGATGTGCCTTTCCCTGCAGTCC  
TTCCATGTGGGAGCAGAGGTGTGAAGAGAATTTACGTGGTTGTGATGCCAAAATCACAGAAC  
AGAATTTCATAGCCAGGCTGCCGTGTTGTTTGAAGTCTCAGAAGGCCCTTCTACTTCAGTTTTG  
AATCCACAAAGAATTAATAACTGGTAACACCACAGGCTTTCTGACCATCCATTTCGTTGGGTT  
TTGCATTTGACCCAACCTCTGCCTACCTGAGGAGCTTTCTTTGGAAACCAGGATGGAACT  
TCTTCCCTGCCTTACCTTCCTTTCACTCCATTCAATTGTCTCTCTGTGTGCAACCTGAGCTG  
GGAAAGGCATTTGGATGCCTCTCTGTTGGGGCCTGGGGCTGCAGAACACACCTGCGTTTCAC  
TGGCCTTCATTAGGTGGCCCTAGGGAGATGGCTTTCTGCTTTGGATCACTGTTCCCTAGCAT  
GGGTCTTGGGTCTATTGGCATGTCCATGGCTTCCCAATCAAGTCTCTTCAAGCCCTCAGTG  
AAGTTTGGCTAAAGGTTGGTGTAAAAATCAAGAGAAGCCTGGAAGACATCATGGATGCCATG  
GATTAGCTGTGCAACTGACCAGCTCCAGGTTTGTATCAAACCAAAGCAACATTTGTATGTG  
GTCTGACCATGTGGAGATGTTTCTGGACTTGCTAGAGCCTGCTTAGCTGCATGTTTGTAGT  
TACGATTTTTGGAATCCCACTTTGAGTGCTGAAAGTGTAAAGGAAGCTTTCTTCTTACACCT  
GGGCTTGGATATTGCCCAGAGAAGAAATTTGGCTTTTTTTTTCTTAATGGACAAGAGACAGT  
TGCTGTTCTCATGTTCCAAGTCTGAGAGCAACAGACCCCTCATCATCTGTGCCTGGAAGAGTT  
CACTGTCAATTGAGCAGCACAGCCTGAGTGCTGGCCTCTGTCAACCCTTATTCCACTGCCTTA  
TTTGACAAGGGGTTACATGCTGCTCACCTTACTGCCCTGGGATTAAATCAGTTACAGGCCAG  
AGTCTCCTTGGAGGGCCTGGAACCTCTGAGTCCTCCTATGAACCTCTGTAGCCTAAATGAAAT  
TCTTAAATCACCGATGGAACCAAAAAAAAAAAAAAAAAAGGGCGGCCGCGACTCTAGAGTCG  
ACCTGCAGTAGGGATAACAGGGTAATAAGCTTGGCCGCCATGG

**FIGURE 153**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50911  
><subunit 1 of 1, 348 aa, 1 stop  
><MW: 39711, pI: 8.70, NX(S/T): 1  
MAATLGPLGSWQQWRRCLSARDGSRMLLLLLLLGSGQGPQQVGAGQTFEYLKREHSLSKPYQ  
GVGTGSSSLWNLMGNAMVMTQYIRLTQPMQSKQ GALWNRVPCFLRDWELQVHFKEHGQKKN  
LHGDGLAIWYTKDRMQPGPVFGNMDKFVGLGVFVDTPNEEKQQERVFPYISAMVNNGSLSY  
DHERDGRPTLGGCTAIVRNLHYDTFLVIRYVKRHLTIMMDIDGKHEWRDCIEVPGVRLPRG  
YYFGTSSITGDLSDNHDVISLKLFEFTVERTPEEEKLHRDVF LPSVDNMKLPENTAPLPPLS  
GLALFLIVFFSLVFSVFAIVIGIILYNKWQEQSRKRFY

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**FIGURE 154**

CCGAGCCGGGCGCGCAGCGACGGAGCTGGGGCCGGCCTGGGACCATGGGCGTGAGTGCAATC  
TACGGATCAGTCTCTGATGGTGGGTCGTTAACCTCAGTGGGGACTCCAAGATTTCATGAAG  
AAAATCAGTTGTCTTCATTCAAGAATTGGGGTCTGGCTCAGAATTCCTGCAGCTGGTGAAAA  
TCTGTTTTCTAGAAGAGGTTTAATTAATGCCTGCAGTCTGACATGTTCCCGATTGAGGTGA  
AACCATGAAGAGAAAAATAGAATACTTAATAATGCTTTTCCGCAACCGCTTCTTGCTGCTGCT  
GGCCCTGGCTGCGCTGCTGGCCTTTGTGAGCCTCAGCCTGCAGTCTTCCACCTGATCCCGG  
TGTCGACTCCTAAGAATGGAATGAGTAGCAAGAGTCGAAAGAGAATCATGCCCCGACCCTGTG  
ACGGAGCCCCCTGTGACAGACCCCGTTTATGAAGCTCTTTTGTACTGCAACATCCCCAGTGT  
GGCCGAGCGCAGCATGGAAGGTCATGCCCCGCATCATTTTAAGCTGGTCTCAGTGCATGTGT  
TCATTGCCCCAGGAGACAGGTACCCACTGTATGTCAATCCCAAACAAAGCGACCAGAAATT  
GACTGCACTCTGGTGGCTAACAGGAAACCGTATCACCCAAACTGGAAGCTTTCATTAGTCA  
CATGTCAAAGGATCCGGAGCCTCTTTCGAAAGCCCCCTGAACTCCTTGCCCTCTTACCCAA  
ATCACCCATTGTGTGAGATGGGAGAGCTCACACAGACAGGAGTTGTGCAGCATTTCAGAAC  
GGTCAGCTGCTGAGGGATATCTATCTAAAGAAACACAAACTCCTGCCCAATGATTGGTCTGC  
AGACCAGCTCTATTTAGAGACCACTGGGAAAAAGCCGACCCTACAAAGTGGGCTGGCCTTGC  
TTTATGGCTTTCTCCAGATTTTGACTGGAAGAAGATTATTTTCAGGCACCAGCCAAGTGCG  
CTGTTCTGCTCTGGAAGCTGCTATTGCCCGGTAAGAAACAGTATCTGGAAAAGGAGCAGCG  
TCGTACGTACCTCCTACGTTTGAAAAACAGCCAGCTGGAGAAGACCTACGGGGAGATGGCCA  
AGATCGTGGATGTCCCCACCAAGCAGCTTAGAGCTGCCAACCCCATAGACTCCATGCTCTGC  
CACTTCTGCCACAATGTGAGCTTTCCCTGTACCAGAAATGGCTGTGTTGACATGGAGCACTT  
CAAGGTAATTAAGACCCATCAGATCGAGGATGAAAGGGAAAGACGGGAGAAGAAATTGTACT  
TCGGGTATTCTCTCCTGGGTGCCACCCCATCCTGAACCAAACCATCGGCCGGATGCAGCGT  
GCCACCGAGGGCAGGAAAGAAGAGCTCTTTGCCCTCTACTCTGCTCATGATGTCACTCTGTC  
ACCAGTTCTCAGTGCCTTGGGCCTTTTCAAGCCAGGTTCCCAAGGTTGCAGCCAGGTTGA  
TCTTTGAGCTTTGGCAAGACAGAGAAAAGCCCAGTGAACATTCCGTCCGGATTCTTTACAAAT  
GGCGTCGATGTCACATTCCACACCTCTTTCTGCCAAGACCACCACAAGCGTTCTCCCAAGCC  
CATGTGCCCGCTTGAAAACCTTGGTCCGCTTTGTGAAAAGGGACATGTTTGTAGCCCTGGGTG  
GCAGTGGTACAAATTATTATGATGCATGTACAGGGAAGGATTCTAAAAGGTATGCAGTACA  
CCAGTATAGAATCCATGCCAATACAGAGCATAGGGAAAGGTCCACTTCTAGTTTGTCTGTT  
ACTAAGGGTAGAAGATTATTGCTTTTTAAAGGCTAAATATTGTTTGTGGGAACCACAGATGG  
TTGGGGTTGAACAGTAAGCACATTGCTGCAATGTGGTACGTGAATTGCTTGGTACAAATGG  
CCAGTTCACAGAGGAATAGAAGGTACTTTATCATAGCCAGACTTCGCTTAGAATGCCAGAAT  
AATATAGTTCAAGACCTGAAGTTGCCAATCCAAGTTTGCACCTCTTCTGGCCTGCCCCATGTT  
ACTATGTGATGGAACCAGCACACCTCAACCAAAATTTTTTAATCTTAGACATTTTACCTT  
GTCCTTGTTAAGAATTTCTTGAAGTGATTTATCTAAATAAAGGTTGGCAAACCTTTTTCTGT  
AAAGGGCCAGATTGTAAATATTTTCAAGCTGTGTGGACCAAAAGGCCACATACAGTCTCTGTC  
ATAACTACTCAACTCTGTTTCTGAAGCAGGAAAGCCACCACAGACAGTACATAAAGGAATAT  
GTGTAGCTGGGTTCAGGCCAGACAAAACAGATGGTGACCAGACTTGGCCCCCTGGGCTGTA  
GTTTGCTGACCCCTCATCTAAAAAATAGGCTATACTACAATTGCACTTCCAGCACTTTGAGA  
ACGAGTTGAATACCAAGAATTATTCAATGGTTCCTCCAGTAACTTCTGCTAGAAACACAGAA  
TTTGGTCTGTATCTGACACTAGAACAAAACCTTGAGGGTAAATAAACATTGAATTAGAATGAA  
TCATAGAAAACCTGATTAGAAGAATACTTGATGTTTATGATGATTGTGGTACAAGATAGTTTT  
AAGTATGTTCTAAATATTTGTCTGCTGAGTCTATTTGCTGTATATGCTGAAATTTTGTAT  
GCCATTTAGTATTTTATAGTTTAGGAAAATATTTCTAAGACCAGTTTTAGATGACTCTTA  
TTCCTGTAGTAATATTCAATTTGCTGTACCTGCTTGGTGGTTAGAAGGAGGCTAGAAGATGA  
ATTCAGGCACCTTCTTCCAATAAACTAATTATGGCTCATTCCCTTGACAAGCTGTAGAAC  
TGGATTCATTTTTAAACCATTTTCATCAGTTTCAATGGTAAATTCTGATTGATTTTTAAAT  
GCGTTTTTGAAGAACCTTTGCTATTAGGTAGTTTACAGATCTTTATAAGGTGTTTTATATAT  
TAGAAGCAATTATAATTACATCTGTGATTTCTGAACATAATGGTGCTAATTCAGAGAAATGGA  
AAGTGAAAGTGAGATTCTCTGTTGTATCGGCATTCCAACTTTTTCTCTTTGTTTGTCCA  
GTGTTGCATTTGAATATGTCTGTTTCTATAAATAAATTTTTTAAGAATAA

**FIGURE 155**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48329  
><subunit 1 of 1, 480 aa, 1 stop  
><MW: 55240, pI: 9.30, NX(S/T): 2  
MLFRNRFLLLLALALAALLAFVSLSLQFFHLIPVSTPKNGMSSKSRKRIMPDPVTEPPVTDVPY  
EALLYCNIPPSVAERSMEGHAPHHFKLVSVHVFIRHGDRYPLYVIPKTKRPEIDCTLVANRKP  
YHPKLEAFISHMSKSGSGASFESPLNSLPLYPNHPLCEMGELTQTGVVQHLQNGQLLRDIYLK  
KHKLLPNDWSADQLYLETTGKSRTLQSGLALLYGFLPDFDWKKIYFRHQPSALFCSGSCYCP  
VRNQYLEKEQRRQYLLRLKNSQLEKTYGEMAKIVDVPTKQLRAANPIDSMMLCHFCHNVSFPC  
TRNGCVDMEHFKVIKTHQIEDERERREKKLYFGYSLLGAHPILNQTIGRMQRATEGRKEELF  
ALYSAHDVTLSPVLSALGLSEARFPRFAARLIFELWQDREKPSEHSVRILYNGVDVTFHTSF  
CQDHHKRSPKPMCPLENLVRFVKRDMFVALGGSGTNYYDACHREGF

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**FIGURE 156**

AAAAAAGCTCACTAAAGTTTCTATTAGAGCGAATACGGTAGATTTCCATCCCCTTTTGAAGA  
ACAGTACTGTGGAGCTATTTAAGAGATAAAAACGAAATATCCTTTCTGGGAGTTCAAGATTG  
TGCAGTAATTGGTTAGGACTCTGAGCGCCGCTGTTACCAATCGGGGAGAGAAAAGCGGAGA  
TCCTGCTCGCCTTGCACGCGCCTGAAGCACAAAGCAGATAGCTAGGAATGAACCATCCCTGG  
GAGTATGTGGAACAACGGAGGAGCTCTGACTTCCCAACTGTCCCATTCTATGGGCGAAGGA  
ACTGCTCCTGACTTCAGTGGTTAAGGGCAGAATTGAAAATAATTCTGGAGGAAGATAAGAAAT  
GATTCCCTGCGCGACTGCACCGGGACTACAAAGGGCTTGTCTGCTGGGAATCCTCCTGGGGA  
CTCTGTGGGAGACCGGATGCACCCAGATACGCTATTAGTTCCGGAAGAGCTGGAGAAAGGC  
TCTAGGGTGGGCGACATCTCCAGGGACCTGGGGCTGGAGCCCCGGGAGCTCGCGGAGCGCGG  
AGTCCGCATCATCCCAGAGGTAGGACGCAGCTTTTCGCCCTGAATCCGCGCAGCGGCAGCT  
TGGTCACGCGGGCAGGATAGACCGGGAGGAGCTCTGTATGGGGGCCATCAAGTGTCAATTA  
AATCTAGACATTCTGATGGAGGATAAAGTGAATAATATGGAGTAGAAGTAGAAGTAAGGA  
CATTAAACGACAATGCGCCTTACTTTCTGTAAGTGAATTAGAAATAAAAATAGTGAAAATG  
CAGCCACTGAGATGCGGTTCCCTCTACCCACGCCTGGGATCCGGATATCGGGAAGAACTCT  
CTGCAGAGCTACGAGCTCAGCCCCGAACACTCACTTCTCCCTCATCGTGCAAAATGGAGCCGA  
CGGTAGTAAGTACCCCCGAATTGGTGCTGAAACGCGCCCTGGACCGCAAGAAAAGGCTGCTC  
ACCACCTGGTCCTTACGGCCTCCGACGGGGGCGCACCCGGTGCGCACAGGCACCGCGCGCATC  
CGCGTGATGGTTCTGGATGCGAACGACAACGCACCAGCGTTTGCTCAGCCCGAGTACCGCGC  
GAGCGTTCCGGAGAATCTGGCCTTGGGCACGCAGCTGCTTGTAGTCAACGCTACCGACCCCTG  
ACGAAGGAGTCAATGCGGAAGTGAGGTATTCTTCCGGTATGTGGACGACAAGCGCGCCCAA  
GTTTTCAAAGTAGATTGTAATTCAGGGACAATATCAACAATAGGGGAGTTGGACCACGAGGA  
GTCAGGATTCTACCAGATGGAAGTGCAAGCAATGGATAATGCAGGATATTCTGCGCGAGCCA  
AAGTCCTGATCACTGTTCTGGACGTGAACGACAATGCCCCAGAAGTGGTCCTCACCTCTCTC  
GCCAGCTCGGTTCCCGAAAACCTCTCCAGAGGGACATTAATTGCCCTTTTAAATGTAAATGA  
CCAAGATTCTGAGGAAAACGGACAGGTGATCTGTTTCATCCAAGGAAATCTGCCCTTTAAAT  
TAGAAAAATCTTACGGAAATTACTATAGTTTAGTCACAGACATAGTCTTGGATAGGGAACAG  
GTTCTTAGCTACAACATCACAGTGACCGCCACTGACCGGGGAACCCCGCCCTATCCACGGA  
AACTCATATCTCGCTGAACGTGGCAGACACCAACGACAACCCGCGCGTCTTCCCTCAGGCCT  
CCTATTCCGCTTATATCCCAGAGAACAATCCAGAGGAGTTTCCCTCGTCTCTGTGACCGCC  
CACGACCCCGACTGTGAAGAGAACGCCCAGATCACTTATTCCCTGGCTGAGAACACCATCCA  
AGGGGCAAGCCTATCGTCCTACGTGTCCATCAACTCCGACACTGGGGTACTGTATGCGCTGA  
GCTCCTTCGACTACGAGCAGTTCCGAGACTTGCAAGTGAAAGTGATGGCGCGGGACAACGGG  
CACCCGCCCCCTCAGCAGCAACGTGTCGTTGAGCCTGTTTCGTGCTGGACCAGAACGACAATGC  
GCCCCAGATCCTGTACCCCGCCCTCCCCACGGACGGTTCCACTGGCGTGGAGCTGGCTCCCC  
GCTCCGAGAGCCCGGCTACCTGGTGACCAAGGTGGTGGCGGTGGACAGAGACTCCGGCCAG  
AACGCCTGGCTGTCTTACCGTCTGCTCAAGGCCAGCGAGCCGGGACTCTTCTCGGTGGGTCT  
GCACACGGGGCAGGTGCGCACGGCGCGAGCCCTGCTGGACAGAGACGCGCTCAAGCAGAGCC  
TCGTAGTGGCCGTCCAGGACCACGGCCAGCCCCCTCTCTCCGCCACTGTCACGCTCACCGTG  
GCCGTGGCCGACAGCATCCCCAAGTCTTGGCGGACCTCGGCAGCCTCGAGTCTCCAGCTAA  
CTCTGAAACCTCAGACCTCACTCTGTACCTGGTGGTAGCGGTGGCCGCGGTCTCCTGCGTCT  
TCCTGGCCTTTCGTATCTTGTGCTGGCGCTCAGGCTGCGGCGCTGGCACAAGTCACGCCTG  
CTGCAGGCTTCAGGAGGCGGCTTGACAGGAGCGCGGCGTGCAGTCTTGTGGGCGTGGACGG  
GGTGCAGGCTTTCCTGCAGACCTATTCCACGAGGTTTCCCTCACCACGGACTCGCGGAAGA  
GTCACCTGATCTTCCCCAGCCCAACTATGCAGACATGCTCGTCAGCCAGGAGAGCTTTGAA  
AAAAGCGAGCCCCTTTTGCTGTGAGGTGATTCCGTATTTTCTAAAGACAGTCATGGGTAAAT  
TGAGGTGAGTTTATATCAAATCTTCTTTTCTTTTCTTTTAAATTGCTCTGTCTCCCAAGCTG  
GAGTGCAGCGGTACGATCATAGCTCACTGCGGCCTCAAACCTCCTAGGCTCAAGCAATTATCC  
CACCTTTGCCTCCGGTGTAAACAGGACTACAGGTGCAAGCCACCTACTGTCTGCCTATCTAT  
CTATCTATCTATCTATCTATCTATCTATCTATCTATCTATTACTTTCTTGTACAGACG  
GGAGTCTCACGCTGTAAATCCAGTACTTTGGGAGGCGGAGGCGGGTGGATCACCTGAGGTT  
GGGAGTTTGAGACCAGCCTGACCAACATGGAGAAACCCCGTCTATACTAAAAAATACAAAA  
TTAGCCGGGCGTGGTGGTGCATGTCTGTAATCCAGCTACTTGGGAGGCTGAGTCAGGAGAA  
TTGCTTTAACTGGGAGGTGGAGGTTGCAATGAGCTGAGATTGTGCCATTGCACTCCAGCCT  
GGGCAACAAGAGTGAAACTCTATCTCA

**FIGURE 157**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48306  
><subunit 1 of 1, 916 aa, 1 stop  
><MW: 100204, pI: 4.92, NX(S/T): 4  
MIPARLHRDYKGLVLLGILLGTLWETGCTQIRYSVPEELEKGSRVGDISRDLGLEPRELAER  
GVRIIPRGRTQLFALNPRSGSLVTAGRIDREELCMGAIKCQLNLDILMEDKVKIYGVEVEVR  
DINDNAPYFRESELEIKISENAATEMRFLPHAWDPDIGKNSLQSYELSPNTHFSLIVQNGA  
DGSKYPELVVKRALDREEKAAHHLVLTASDGGDPVRTGTARIRVMVLDANDNAPAFAPQPEYR  
ASVPENLALGTQLLVVNATDPDEGVNAEVRYSFYVDDKAAQVFKLDCNSGTISTIGELDHE  
ESGFYQMEVQAMDNAGYSARAKVLITVLDVNDNAPEVVLTSLASSVPENSPRGTLIALLVN  
DQDSEENGQVICFIQGNLPFKLEKSYGNYISLVTDIVLDREQVPSYNITVTATDRGTPPLST  
ETHISLNVADTNDNPPVFPQASYSAYIPENNPRGVSLVSVTAHDPDCEENAQITYSLAENTI  
QGASLSSYVSINS DTGVLYALSSFDYEQFRDLQVKVMARDNGHPPLSSNVLSLFLVDQNDN  
APEILYPALPTDGSTGVELAPRSAEPGYLVTKVAVDRDSGQNAWLSYRLLKASEPGLFSVG  
LHTGEVRTARALLDRDALKQSLVVAVQDHGQPPLSATVTLTVAVADSIPOVLADLGSLESPA  
NSETSDLTLYLVVAVAAVSCVFLAFVILLALLRLRRWHKSRLLOASGGGLTGAPASHFVGVD  
GVQAFLOTYSHEVSLTTDSRKSHLIFPQPNYADMLVSQESFEKSEPLLLSGDSVFSKDSHGL  
IEVSLYQIFFLFFNCVSVSQAGVQRYDHSSLRPQTPRLKQLSHLCLRCNRD YRCKPPTVCLS  
IYLSIYLSIYLSIYLLSCTDGS LTPVIPVLWEAEAGGSPEVGS LRPA

**FIGURE 158**

CCCAGGCTCTAGTGCAGGAGGAGAAGGAGGAGGAGCAGGAGGTGGAGATTCCCAGTTAAAAG  
GCTCCAGAATCGTGTACCAGGCAGAGAACTGAAGTACTGGGGCCTCCTCCACTGGGTCCGAA  
TCAGTAGGTGACCCCGCCCCTGGATTCTGGAAGACCTCACCATGGGACGCCCCGACCTCGT  
GCGGCCAAGACGTGGATGTTCTTGCTCTTGCTGGGGGGAGCCTGGGCAGGACACTCCAGGGC  
ACAGGAGGACAAGGTGCTGGGGGGTTCATGAGTGCCAACCCCATTCGCAGCCTTGGCAGGCGG  
CCTTGTTCCAGGGCCAGCAACTACTCTGTGGCGGTGTCCTTGTAGGTGGCAACTGGGTCTT  
ACAGCTGCCCCACTGTAAAAAACCGAAATACACAGTACGCCTGGGAGACCACAGCCTACAGAA  
TAAAGATGGCCCAGAGCAAGAAATACCTGTGGTTCAGTCCATCCCACACCCCTGCTACAACA  
GCAGCGATGTGGAGGACCACAACCATGATCTGATGCTTCTTCAACTGCGTGACCAGGCATCC  
CTGGGGTCCAAAGTGAAGCCCATCAGCCTGGCAGATCATTGCACCCAGCCTGGCCAGAAGTG  
CACCGTCTCAGGCTGGGGCACTGTCACCAAGTCCCCGAGAGAATTTCTGACACTCTCAACT  
GTGCAGAAGTAAAAATCTTTCCCCAGAAGAAGTGTGAGGATGCTTACCCGGGGCAGATCACA  
GATGGCATGGTCTGTGCAGGCAGCAGCAAAGGGGCTGACACGTGCCAGGGCGATTCTGGAGG  
CCCCCTGGTGTGTGATGGTGCCTCCAGGGCATCACATCCTGGGGCTCAGACCCCTGTGGGA  
GGTCCGACAAACCTGGCGTCTATACCAACATCTGCCGCTACCTGGACTGGATCAAGAAGATC  
ATAGGCAGCAAGGGCTGATTTCTAGGATAAGCACTAGATCTCCCTTAATAAACTCACAACTCT  
CTGGTTC

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**FIGURE 159**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48336  
<subunit 1 of 1, 260 aa, 1 stop  
<MW: 28048, pI: 7.87, NX(S/T): 1  
MGRPRPRAAKTWMFLLLLGGAWAGHSRAQEDKVLGGHECQPHSQPWQAALFQGQQLLCGGVL  
VGGNWWLTAAHCKKPKYTVRLGDHSLQNKDGPEQEIPVVQSIPHPCYNSSDVEDHNDLMLL  
QLRDQASLGSKVKPISLADHCTQPGQKCTVSGWGTVTSPRENFDTLNCAEVKIFPQKKCED  
AYPGQITDGMVCAGSSKGADTCQGDGGPLVCDGALQGITSWGS DPCGRSDKPGVYTNICRY  
LDWIKKIIGSKG

**Important Features:****Signal peptide:**

amino acids 1-23

**Transmembrane domain:**

amino acids 51-71

**N-glycosylation site.**

amino acids 110-113

**Serine proteases, trypsin family, histidine active site.**

amino acids 69-74 and 207-217

**Tyrosine kinase phosphorylation site.**

amino acids 182-188

**Kringle domain proteins motif**

amino acids 205-217

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**FIGURE 160**

GGCGCCGGTGCACCGGGCGGGCTGAGCGCCTCCTGCGGCCCGGCCTGCGCGCCCCGGCCCCG  
CGCGCCGCCCACGCCCCAACCCGGCCCGCGCCCCCTAGCCCCCGCCGGGCCCCGCGCCCCG  
GCCCCGCGCCAGGTGAGCGCTCCGCCCCGCGGAGGCCCCGCCCCGGCCCCGCCCCGCCCCG  
CCCCGGCCGGCGGGGGAACGGGCGGATTCTCGCGCGTCAAACCACCTGATCCCATAAAAC  
ATTTCATCTCCCGGCGGCCCGCGCTGCGAGCGCCCCGCCAGTCCGCGCCGCGCCGCCCTCG  
CCCTGTGCGCCCTGCGCGCCCTGCGCACCCGCGGCCCGAGCCAGCCAGAGCCGGGCGGAGC  
GGAGCGCGCCGAGCCTCGTCCCGCGGCCCGGGCCGGGGCCGGGCCGTAGCGGCGGCGCCTGGA  
TGCGGACCCGGCCGCGGGGAGACGGGCGCCCCGCCGAAACGACTTTCAGTCCCCGACGCGC  
CCCGCCCAACCCCTACGATGAAGAGGGCGTCCGCTGGAGGGAGCCGGCTGCTGGCATGGGTG  
CTGTGGCTGCAGGCCTGGCAGGTGGCAGCCCCATGCCAGGTGCCTGCGTATGCTACAATGA  
GCCCAAGGTGACGACAAGCTGCCCCCAGCAGGGCCTGCAGGCTGTGCCCGTGGGCATCCCTG  
CTGCCAGCCAGCGCATCTTCTGTCACGGCAACCGCATCTCGCATGTGCCAGCTGCCAGCTTC  
CGTGCTTGC CGCAACCTCACCATCCTGTGGCTGCACTCGAATGTGCTGGCCCGAATTGATGC  
GGCTGCCTTCACTGGCCTGGCCCTCCTGGAGCAGCTGGACCTCAGCGATAATGCACAGCTCC  
GGTCTGTGGACCCTGCCACATTCACGGCCTGGGCGCCTACACACGCTGCACCTGGACC GC  
TGCGGCCTGCAGGAGCTGGGCCCCGGGGCTGTTCCGCGGCCTGGCTGCCCTGCAGTACCTCTA  
CCTGCAGGACAACGCGCTGCAGGCACTGCCTGATGACACCTTCCGCGACCTGGGCAACCTCA  
CACACCTCTTCTGTCACGGCAACCGCATCTCCAGCGTGCCCCGAGCGCGCCTTCCGTGGGCTG  
CACAGCTCGACCGTCTCCTACTGCACCAAGAACGCGTGCCCCATGTGCACCCGCATGCCTT  
CCGTGACCTTGGCCGCTCATGACACTCTATCTGTTTGCCAACAATCTATCAGCGCTGCCCA  
CTGAGGCCCTGGCCCCCTGCGTGCCCTGCAGTACCTGAGGCTCAACGACAACCCCTGGGTG  
TGTGACTGCCGGGCACGCCCCACTTGGGCCCTGGCTGCAGAAGTTCCGCGGCTCCTCCTCCGA  
GGTGCCCTGCAGCCTCCCGCAACGCTGGCTGGCCGTGACCTCAAACGCCTAGCTGCCAATG  
ACCTGCAGGGCTGCGCTGTGGCCACCGGCCCTTACCATCCCATCTGGACCGGCAGGGCCACC  
GATGAGGAGCCGCTGGGGCTTCCCAAGTGCTGCCAGCCAGATGCCGCTGACAAGGCCTCAGT  
ACTGGAGCCTGGAAGACCAGCTTCGGCAGGCAATGCGCTGAAGGGACGCGTGCCGCCCCGGTG  
ACAGCCCCGCCGGGCAACGGCTCTGGCCCACGGCACATCAATGACTCACCCCTTGGGACTCTG  
CCTGGCTCTGCTGAGCCCCCGCTCACTGCAGTGCGGCCCGAGGGCTCCGAGCCACCAGGGTT  
CCCCACCTCGGGCCCTCGCCGGAGGCCAGGCTGTTACGCAAGAACCGCACCCGACGCCACT  
GCCGTCTGGGCCAGGCAGGCAGCGGGGTGGCGGGACTGGTGACTCAGAAGGCTCAGGTGCC  
CTACCCAGCCTCACCTGCAGCCTCACCCCCCTGGGCCTGGCGCTGGTGCTGTGGACAGTGCT  
TGGGCCCTGCTGACCCCCAGCGGACACAAGAGCGTGCTCAGCAGCCAGGTGTGTGTACATAC  
GGGGTCTCTCTCCACGCCGCCAAGCCAGCCGGGCGGCCGACCCGTGGGGCAGGCCAGGCCAG  
GTCTTCCCTGATGGACGCTGCCGCCCCGCCACCCCATCTCCACCCCATCATGTTTACAGGG  
TTCGGCGGCAGCGTTTGTTCAGAACGCCGCTCCACCCAGATCGCGGTATATAGAGATAT  
GCATTTTATTTTACTTGTGTAATAATATCGGACGACGTGGAATAAAGAGCTCTTTTCTTAA  
AAAA

**FIGURE 161**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA44184  
><subunit 1 of 1, 473 aa, 1 stop  
><MW: 50708, pI: 9.28, NX(S/T): 6  
MKRASAGGSRL LAWVLWLQAWQVAAPCPGACVCYNEPKVTTSCPQQGLQAVPVGIP AASQRI  
FLHG NRISHVPAASFRACRNLTILWLHSNVLARIDAAFTGLALLEQLDLSDNAQLRSVDPA  
TFHGLGR LHTLHLDRCLQELGPGLFRGLAALQYLYLQDNALQALPDDTFRDLGNLTHLFLH  
GNRISSVPERAFRGLHSLDRLLLHQNRVAHVHPHAFRDLGR LMTLYLFANNLSALPTEALAP  
LRALQYLR LNDNPWVCD CRARPLWAWLQKFRGSSSEVP CSLPQRLAGRDLKRLAANDLQGCA  
VATGPYHPIWTGRATDEEPLGLPKCCQPDAA DKASVLEPGRPASAGNALKGRVPPGDSPPGN  
GSGPRHINDSPFGTLPGSAEPPLTAVRPEGSEPPGFPTSGPRRRPGCSRKNRTRSHCRLGQA  
GSGGGGTGDSEGS GALPSLTCSLTPLGLALVLWTVLGPC

**Important features:****Signal peptide:**

amino acids 1-26

**Leucine zipper pattern.**

amino acids 135-156

**Glycosaminoglycan attachment site.**

amino acids 436-439

**N-glycosylation site.**

amino acids 82-85, 179-183, 237-240, 372-375 and 423-426

**VWFC domain**

amino acids 411-425



**FIGURE 162**

GGAAGTCCACGGGGAGCTTGGATGCCAAAGGGAGGACGGCTGGGTCTCTGGAGAGGACTAC  
TCACTGGCATATTTCTGAGGTATCTGTAGAATAACCACAGCCTCAGATACTGGGGACTTTAC  
AGTCCACAGAACCCTCCTCCAGGAAGCTGAATCCAGCAAGAACAATGGAGGCCAGCGGGA  
AGCTCATTTCAGACAAAGGCAAGTCCTTTTTCTCTTTTGGGCTTATCTCTGGCG  
GGCGCGGCGGAACCTAGAAGCTATTCTGTGGTGGAGGAACTGAGGGCAGCTCCTTTGTCAC  
CAATTTAGCAAAGGACCTGGGTCTGGAGCAGAGGGAATTCTCCAGGCGGGGGTtagggTTG  
TTTCAGAGGGGAACAACTACATTTGCAGCTCAATCAGGAGACCGCGGATTGTGTGCTAAAT  
GAGAAATTGGACCGTGAGGATCTGTGCGGTACACAGAGCCCTGTGTGCTACGTTTCCAAGT  
GTTGCTAGAGAGTCCCTTCGAGTTTTTCAAGCTGAGCTGCAAGTAATAGACATAAACGACC  
ACTCTCCAGTATTTCTGGACAAACAATGTTGGTGAAAGTATCAGAGAGCAGTCCTCCTGGG  
ACTACGTTTTCTCTGAAGAATGCCGAAGACTTAGATGTAGGCCAAAACAATATTGAGAACTA  
TATAATCAGCCCCAACTCCTATTTTCGGGTCTCACC CGCAAACGCAGTGATGGCAGGAAAT  
ACCCAGAGCTGGTGTGCTGGACAAAGCGCTGGACCGAGAGGAAGAAGCTGAGCTCAGGTTAACA  
CTCACAGCACTGGATGGTGGCTCTCCGCCAGATCTGGCACTGCTCAGGTCTACATCGAAGT  
CCTGGATGTCAACGATAATGCCCTGAATTTGAGCAGCCTTTCTATAGAGTGCAGATCTCTG  
AGGACAGTCCGGTAGGCTTCTGGTGTGAAGGTCTCTGCCACGGATGTAGACACAGGAGTC  
AACGGAGAGATTTCTTACTTTTCCAAGCTTCAGAAGAGATTGGCAAAACCTTTAAGAT  
CAATCCCTTGACAGGAGAAATTGAACATAAAAAACAACTCGATTTGAAAAACTTCAGTCCT  
ATGAAGTCAATATTGAGGCAAGAGATGCTGGAACCTTTCTGGAAAATGCACCGTTCTGATT  
CAAGTGATAGATGTGAACGACCATGCCCAAGTTACCATGTCTGCATTTACCAGCCCAAT  
ACCTGAGAACCGCGCTGAACTGTGGTTGCACTTTTCAGTGTTCAGATCTTGATTGAGGAG  
AAAATGGGAAAATTAGTTGCTCCATTGAGGAGGATCTACCCTTCTCCTGAAATCCGCGGAA  
AATTTTACACCTACTAACGGAGAGACCCTAGACAGAGAAAGCAGAGCGGAATACAACAT  
CACTATCACTGTCACTGACTTGGGGACCCCTATGCTGATAACACAGCTCAATATGACCGTGC  
TGATCGCCGATGTCAATGACAACGCTCCCGCCTTCACCCAAACCTCCTACACCTGTTCTGTC  
CGCGAGAACACAGCCCCGCCCTGCACATCCGCAGCGTCAGCGCTACAGACAGAGACTCAGG  
CACCAACGCCCAGGTCACCTACTCGCTGCTGCCGCCCAGGACCCGCACCTGCCCTCACAT  
CCCTGGTCTCCATCAACGCGGACAACGGCCACCTGTTCCGCCCTCAGGTCTCTGGACTACGAG  
GCCCTGCAGGCGTTCCAGTTCCGCGTGGGCGCTTCAGACCAGGCTCCCGGCGCTGAGCAG  
CGAGGCGCTGGTGCAGCGTGGTGGTGTGCTGGACGCCAACGACAACCTCGCCCTTCGTGCTGTACC  
CGCTGCAGAACGGCTCCGCGCCCTGCACCGAGCTGGTGCCCCGGGCGGCGGAGCCGGGCTAC  
CTGGTGACCAAGGTGGTGGCGGTGGACGGCGACTCGGGCCAGAACGCCTGGCTGTCTGTACCA  
GCTGCTCAAGGCCACGGAGCTCGGTCTGTTTCGGCGTGTGGGCGCACAATGGCGAGGTGCGCA  
CCGCCAGGCTGCTGAGCGAGCGCGACGCGGCCAAGCACAGGCTGGTGGTGTGGTCAAGGAC  
AATGGCGAGCCTCCGCGCTCGGCCACCGCCACGCTGCACGTGCTCCTGGTGGACGGCTTCTC  
CCAGCCCTACCTGCCTCTCCCGGAGGCGGCCCCGACCCAGGCCCAGGCCGACTTGCTCACCG  
TCTACCTGGTGGTGGCGTTGGCCTCGGTGTCTTCGCTCTTCTCTTTTCGGTGTCTCTGTTC  
GTGGCGGTGCGGCTGTGTAGGAGGAGCAGGGCGGCCTCGGTGGGTGCTGCTTGGTGGCCGA  
GGGCCCCCTTCAGGGCATCTTGTGGACATGAGCGGCACCAGGACCTATCCCAGAGCTACC  
AGTATGAGGTGTGTCTGGCAGGAGGCTCAGGGACCAATGAGTTCAAGTTCTGAAGCCGATT  
ATCCCCAACTTCCCTCCCGAGTGCCCTGGGAAAGAAATACAAGGAAATTCTACCTTCCCCAA  
TAACTTTGGGTTCAATATTAGTGACCATAGTTGACTTTTACATTCCATAGGTATTTTATTT  
TGTGGCATTTCATGCCAATGTTTATTTCCCCCAATTTGTGTGTATGTAATATTGTACGGAT  
TTACTCTTGATTTTTCTCATGTTCTTCTCCCTTGTTTTAAAGTGAACATTTACCTTTATT  
CCTGGTTCTT

**FIGURE 163**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48314  
<subunit 1 of 1, 798 aa, 1 stop  
<MW: 87552, pI: 4.84, NX(S/T): 5  
MEASGKLICRQRQVLFSFLLLGLSLAGAAEPRSYSVVEETEGSSFVTNLAKDLGLEQREFSR  
RGVRVVSARGNKLHLQLNQETADLLLNEKLDREDLCGHTEPCVLRQVLLSPFEFFQAELOV  
IDINDHSPVFLDKQMLVKVSESSPPGTTFPLKNAEDLDVGQNNIENYIISPNSYFRVLTRKR  
SDGRKYPELVLDKALDREEEAELRLTLTALDGGSPPRSGTAQVYIEVLDVNDNAPEFEQPFY  
RVQISEDSPVGFLVVKVSATDVDTGNGEISYSLFQASEEIGKTFKINPLTGEIELKKQLDF  
EKLQSYEVNIEARDAGTFSGKCTVLIQVIDVNDHAPEVTMSAFTSPIPENAPETVVALFSVS  
DLDSGENGKISCSIQEDLPFLLKSAENFYTLTTERPLDRESRAEYNITITVTDLGTPLMITQ  
LNMTVLIADVNDNAPAFQTQTSYTLFVRENNSPALHIRSVSATDRDSGTNAQVTYSLLPPQDP  
HLPLTSLVSINADNGHLFALRSLDYEQFQFRVGASDHGSPALSSEALVRVVVLDANDNS  
PFVLYPLONGSAPCTELVPRAAEPGYLVTKVAVDGDGQNAWLSYQLLKATELGFLGVWAH  
NGEVRTARLLSERDAAKHRLVVLVKDNGEPPRSATATLHVLLVDGFSQPYLPLPEAAPTQQA  
ADLLTVYLVVALASVSSLEFLFSVLLFVAVRLCRRSRAASVGRCLVPEGPLPGHLVDMSGTRT  
LSQSYQYEVCLAGSGTNEFKFLKPIIPNFPPQCPGKEIQGNSTFPNNFGFNIQ

**Important features:****Signal peptide:**

amino acids 1-26

**Transmembrane domain:**

amino acids 685-712

**Cadherins extracellular repeated domain signature.**

amino acids 122-132, 231-241, 336-346, 439-449 and 549-559

**ATP/GTP-binding site motif A (P-loop).**

amino acids 285-292

**N-glycosylation site.**

amino acids 418-421, 436-439, 567-570 and 786-789

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**FIGURE 164**

ACCCACGCGTCCGCCCACGCGTCCGCCCACGCGTCCGCCCACGCGTCCGCGCGTAGCCGTGC  
GCCGATTGCCTCTCGGCCTGGGCAATGGTCCCGGCTGCCGGTCGACGACCGCCCCGCGTCAT  
GCGGCTCCTCGGCTGGTGGCAAGTATTGCTGTGGGTGCTGGGACTTCCCGTCCGCGGCGTGG  
AGGTTGCAGAGGAAAGTGGTCGCTTATGGTCAGAGGAGCAGCCTGCTCACCCTCTCCAGGTG  
GGGGCTGTGTACCTGGGTGAGGAGGAGCTCCTGCATGACCCGATGGGCCAGGACAGGGCAGC  
AGAAGAGGCCAATGCGGTGCTGGGGCTGGACACCCAAGGCGATCACATGGTGATGCTGTCTG  
TGATTCCCTGGGGAAGCTGAGGACAAAGTGAGTTCAGAGCCTAGCGGCGTCACCTGTGGTGCT  
GGAGGAGCGGAGGACTCAAGGTGCAACGTCCGAGAGAGCCTTTTCTCTCTGGATGGCGCTGG  
AGCACACTTCCCTGACAGAGAAGAGGAGTATTACACAGAGCCAGAAGTGGCGGAATCTGACG  
CAGCCCCGACAGAGGACTCCAATAACACTGAAAGTCTGAAATCCCCAAAGGTGAACTGTGAG  
GAGAGAAACATTACAGGATTAGAAAATTTCACTCTGAAAATTTTAAATATGTCACAGGACCT  
TATGGATTTTCTGAACCCAAACGGTAGTGACTGTACTCTAGTCCTGTTTTACACCCCGTGGT  
GCCGCTTTTCTGCCAGTTTGGCCCCCTCACTTTAACTCTCTGCCCCGGGCATTTCCAGCTCTT  
CACTTTTTGGCACTGGATGCATCTCAGCACAGCAGCCTTTCTACCAGGTTTGGCACCGTAGC  
TGTTCCCTAATATTTTATTATTTCAAGGAGCTAAACCAATGGCCAGATTTAATCATAACAGATC  
GAACACTGGAAACACTGAAAATCTTCATTTTAAATCAGACAGGTATAGAAGCCAAGAAGAAT  
GTGGTGGTAACTCAAGCCGACCAATAGGCCCTCTTCCCAGCACTTTGATAAAAAGTGTGGA  
CTGGTTGCTTGTATTTTCTTATTCTTTTAAATTAGTTTTATTATGTATGCTACCATTTCGAA  
CTGAGAGTATTCGGTGGCTAATTCCAGGACAAGAGCAGGAACATGTGGAGTAGTGATGGTCT  
GAAAGAAGTTGCAAGAGGAACTTCAATCCTTCGTTTCAGAAATAGTGCTACAGTTTCATA  
CATTTTCTCCAGTGACGTGTTGACTTGAACTTCAGGCAGATTAAAAGAATCATTTGTTGAA  
CAACTGAATGTATAAAAAAATTATAAACTGGTGTTTTAACTAGTATTGCAATAAGCAAATGC  
AAAAATATTCAATAG

**FIGURE 165**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48333  
><subunit 1 of 1, 360 aa, 1 stop  
><MW: 39885, pI: 4.79, NX(S/T): 7  
MVPAAGRRPPRVMRLLGWWQVLLWVLGLPVRGVEVAEESGRLWSEEQPAHPLQVGAVYLGEE  
ELLHDPMGQDRAAEEANAVLGLDTQGDHVMVLSVIPGEAEDKVSSEPSGVTCGAGGAEDSRC  
NVRESLFSLDGAGAHFPDREEEYYTEPEVAESDAAPTEDSNNTESLKSPKVNCEERNITGLE  
NFTLKILNMSQDLMDFLNPNGSDCTLVLFYTPWCRFSASLAPHFNSLPRAFPALHFLALDAS  
QHSSLSTRFGTVAVPNILLFQGAKPMAFNHTDRTLETCLKIFIFNQTGIEAKKNVVVTQADQ  
IGPLPSTLIKSVDWLLVFSLEFLISFIMYATIRTESIRWLIPGQEQEHVE

**Important features:****Signal peptide:**

amino acids 1-25

**Transmembrane domain:**

amino acids 321-340

**Homologous region to dilsufide isomerase**

amino acids 212-302

**N-glycosylation site.**amino acids 165-168, 181-184, 187-190, 194-197, 206-209, 278-281  
and 293-296**Thioredoxin domain**

amino acids 211-227

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**FIGURE 166**

CCCGGCTCCGCTCCCTCTGCCCCCTCGGGGTGCGCGCCCCACGATGCTGCAGGGCCCTGGCT  
CGCTGCTGCTGCTCTTCCTCGCCTCGCACTGCTGCCTGGGCTCGGCGCGGGGCTCTTCCTC  
TTTGGCCAGCCCGACTTCTCCTACAAGCGCAGCAATTGCAAGCCCATCCCGGTCAACCTGCA  
GCTGTGCCACGGCATCGAATACCAGAACATGCGGCTGCCAACCTGCTGGGCCACGAGACCA  
TGAAGGAGGTGCTGGAGCAGGCCGGCGCTTGGATCCCGCTGGTCATGAAGCAGTGCCACCCG  
GACACCAAGAAGTTCTGTGCTCGCTCTTCGCCCCCGTCTGCCTCGATGACCTAGACGAGAC  
CATCCAGCCATGCCACTCGCTCTGCGTGACAGGTGAAGGACCGCTGCGCCCCGGTTCATGTCCG  
CCTTCGGCTTCCCCTGGCCCGACATGCTTGAGTGCGACCGTTTCCCCCAGGACAACGACCTT  
TGCATCCCCCTCGCTAGCAGCGACCACCTCCTGCCAGCCACCGAGGAAGCTCCAAAGGTATG  
TGAAGCCTGCAAAAATAAAAATGATGATGACAACGACATAATGGAAACGCTTTGTAAAATG  
ATTTTGCACTGAAAATAAAAGTGAAGGAGATAACCTACATCAACCGAGATACCAAAATCATC  
CTGGAGACCAAGAGCAAGACCATTTACAAGCTGAACGGTGTGTCCGAAAGGGACCTGAAGAA  
ATCGGTGCTGTGGCTCAAAGACAGCTTGCAGTGCACCTGTGAGGAGATGAACGACATCAACG  
CGCCCTATCTGGTCATGGGACAGAAACAGGGTGGGGAGCTGGTGATCACCTCGGTGAAGCGG  
TGGCAGAAGGGGCAGAGAGAGTTCAAGCGCATCTCCCGCAGCATCCGCAAGCTGCAGTGCTA  
GTCCCGGCATCCTGATGGCTCCGACAGGCCTGCTCCAGAGCACGGCTGACCATTTCTGCTCC  
GGGATCTCAGCTCCCGTTCCCCAAGCACACTCCTAGCTGCTCCAGTCTCAGCCTGGGCAGCT  
TCCCCCTGCCTTTTGCACGTTTGCATCCCCAGCATTTCTTGAGTTATAAGGCCACAGGAGTG  
GATAGCTGTTTTACCTAAAGGAAAAGCCCCACCCGAATCTTGTAGAAATATTCAAACATAA  
AAATCATGAATATTTTAA

**FIGURE 167**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50920  
><subunit 1 of 1, 295 aa, 1 stop  
><MW: 33518, pI: 7.74, NX(S/T): 0  
MLQGPGSLLLLFLASHCCLGSARGLFLFGQPDFSYKRSNCKPIPVNLQLCHGIEYQNMRLPN  
LLGHETMKEVLEQAGAWIPLVMKQCHPDTKKFLCSLFAPVCLDDLDETIQPCHSLCVQVKDR  
CAPVMSAFGFPWPDMLECDRFPQDNDLCIPLASSDHLLPATEEAPKVCEACKNKNDDNDNDIM  
ETLCKNDFALKIKVKEITYINRDTKIILETKSKTIYKLNGVSEKDLKKSVLWLKDSLQCTCE  
EMNDINAPYLVMGQKQGGEVLVITSVKRWQKGQREFKRISRSIRKLQC

**Important features:**

**Signal peptide:**

amino acids 1-20

**Cysteine rich domain, homologous to frizzled N terminus**

amino acids 6-153

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**FIGURE 168**

GTGGAGGCCCGCCGACGATGGCGGGGCCGACGGAGGCCGAGACGGGGTTGGCCGAGCCCCGGG  
CCCTGTGCGCGCAGCGGGGCCACCGCACCTACGCGCGCCGCTGGGTGTTCTGCTCGCGATC  
AGCCTGCTCAACTGCTCCAACGCCACGCTGTGGCTCAGCTTTGCACCTGTGGCTGACGTCAT  
TGCTGAGGACTTGGTCCTGTCCATGGAGCAGATCAACTGGCTGTCACTGGTCTACCTCGTGG  
TATCCACCCCATTTGGCGTGGCGGCCATCTGGATCCTGGACTCCGTCGGGCTCCGTGCGGCG  
ACCATCCTGGGTGCGTGGCTGAACTTTGCCGGGAGTGTGCTACGCATGGTGCCCTGCATGGT  
TGTTGGGACCCAAAACCCATTTGCCCTTCTCATGGGTGGCCAGAGCCTCTGTGCCCTTGCC  
AGAGCCTGGTCATCTTCTCTCCAGCCAAGCTGGCTGCCTTGTGGTTCCCAGAGCACCAGCGA  
GCCACGGCCAACATGCTCGCCACCATGTGCAACCCTCTGGGCGTCCTTGTGGCCAATGTGCT  
GTCCCCTGTGCTGGTCAAGAAGGGTGAGGACATTCCGTTAATGCTCGGTGTCTATACCATCC  
CTGCTGGCGTCGTCTGCCTGCTGTCCACCATCTGCCTGTGGGAGAGTGTGCCCCCACCCTG  
CCCTCTGCCGGGGCTGCCAGCTCCACCTCAGAGAAGTTCCTGGATGGGCTCAAGCTGCAGCT  
CATGTGGAACAAGGCCTATGTCATCCTGGCTGTGTGCTTGGGGGGAATGATCGGGATCTCTG  
CCAGCTTCTCAGCCCTCCTGGAGCAGATCCTCTGTGCAAGCGGCCACTCCAGTGGGTTTTCC  
GGCCTCTGTGGCGCTCTCTTCATCACGTTTGGGATCCTGGGGGCACTGGCTCTCGGCCCTA  
TGTGGACCGGACCAAGCACTTCACTGAGGCCACCAAGATTGGCCTGTGCCTGTTCTCTCTGG  
CCTGCGTGCCCTTTGCCCTGGTGTCCCAGCTGCAGGGACAGACCCTTGCCCTGGCTGCCACC  
TGCTCGCTGCTCGGGCTGTTTGGCTTCTCGGTGGGCCCCGTGGCCATGGAGTTGGCGGTCTGA  
GTGTTCTTCCCCGTGGGGGAGGGGGCTGCCACAGGCATGATCTTTGTGCTGGGGCAGGCCG  
AGGGAATACTCATCATGCTGGCAATGACGGCACTGACTGTGCGACGCTCGGAGCCGTCTTG  
TCCACCTGCCAGCAGGGGGAGGATCCACTTGACTGGACAGTGTCTCTGCTGCTGATGGCCGG  
CCTGTGCACCTTCTTCAGCTGCATCCTGGCGGTCTTCTTCCACACCCCATACCGGCGCTGC  
AGGCCGAGTCTGGGGAGCCCCCTCCACCCGTAACGCCGTGGGCGGCGCAGACTCAGGGCCG  
GGTGTGGACCGAGGGGGAGCAGGAAGGGCTGGGGTCTGGGGCCCAGCACGGCGACTCCGGA  
GTGCACGGCGAGGGGGGCTCGCTAGAGGACCCAGAGGGCCCGGAGCCCCCACCAGCCT  
GCCACCGAGCGACTCCCCGTGCGCAAGGCCAGCAGCCACCGACGCGCCCTCCCGCCCCGGC  
AGACTCGCAGGCAGGGTCCAAGCGTCCAGGTTTATTGACCCGGCTGGGTCTCACTCCTCCTT  
CTCCTCCCCGTGGGTGATCACGTAGCTGAGCGCCTTGTAGTCCAGGTTGCCCGCCACATCGA  
TGGAGGCGAACTGGAACATCTGGTCCACCTGCGGGCGGGGGCGAAAGGGCTCCTTGCGGGCT  
CCGGGAGCGAATTACAAGCGCGCACCTGAAAA

**FIGURE 169**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50988  
><subunit 1 of 1, 560 aa, 1 stop  
><MW: 58427, pI: 6.86, NX(S/T): 2  
MAGPTEAETGLAEPRALCAQRGHRTYARRWVFLLAISLLNCSNATLWLSFAPVADVIAEDLV  
LSMEQINWLSLVYLVVSTPFGVAIWILDSVGLRAATILGAWLNFAGSVLRMVPCLMVVGTON  
PFAFLMGGQSLCALAQSLVIFSPAKLAALWFPEHQ RATANMLATMSNPLGVLVANVLSPVLV  
KKGEDIPMLLGVYTIPAGVVCLLSTICLWESVPPTPPSAGAASSTSEKFLDGLKLQLMWNKA  
YVILAVCLGGMIGISASFALLEQILCASGHSSGFSGLCGALFITFGILGALALGPYVDRTK  
HFTEATKIGLCLFSLACVPFALVSQLOGQTLALAATCSLLGLFGFSVGPVAMELAVECSFPV  
GEGAATGMIFVLGQAEGILIMLALTVRSEPSLSTCQOGEDPLDWTVSLLL MAGLCTFF  
SCILAVFFHTPYRRLQAESGEPPTSTRNAVGGADSGPGVDRGGAGRAGVLGPSTATPECTARG  
ASLEDPRGPGSPHPACHRATPRAQGAATDAPSRPGRLAGRVQASRFIDPAGSHSSFSPWVIT

**Important features:****Potential Transmembrane domains:**

amino acids 30-50, 61-79, 98-112, 126-146, 169-182, 201-215, 248-  
268, 280-300, 318-337, 341-357, 375-387, 420-441

**N-glycosylation site.**

amino acids 40-43 and 43-46

**Glycosaminoglycan attachment site.**

amino acids 468-471



**FIGURE 170A**

GTCCACATCCTGCTCAACTGGGTCAGGTCCCTCTTAGACCAGCTCTTGTCCATCATTGCT  
GAAGTGGACCAACTAGTTCCCCAGTAGGGGGTCTCCCCTGGCAATTCTTGATCGGCGTTTGG  
ACATCTCAGATCGCTTCCAATGAAGATGGCCTTGCCTTGGGGTCCTGCTTGTTCATAATCA  
TCTAACTATGGGACAAGGTTGTGCCGGCAGCTCTGGGGGAAGGAGCACGGGGCTGATCAAGC  
CATCCAGGAAACACTGGAGGACTTGTCCAGCCTTGAAAGAACTCTAGTGGTTTCTGAATCTA  
GCCCCTTGGCGGTAAGCATGATGCAACTTCTGCAACTTCTGCTGGGGCTTTTGGGGCCAGG  
TGGCTACTTATTTCTTTTAGGGGATTGTGAGGAGGTGACCACTCTCACGGTGAAATACCAAG  
TGTCAGAGGAAGTGCCATCTGGTACAGTGATCGGGAAGCTGTCCAGGAACTGGGCCGGGAG  
GAGAGGCGGAGGCAAGCTGGGGCCGCCTTCCAGGTGTTGCAGCTGCCTCAGGCGCTCCCCAT  
TCAGGTGGACTCTGAGGAAGGCTTGCTCAGCACAGGCAGGCGGTGGATCGAGAGCAGCTGT  
GCCGACAGTGGGATCCCTGCCTGGTTTCTTTGATGTGCTTGCCACAGGGGATTTGGCTCTG  
ATCCATGTGGAGATCCAAGTGCTGGACATCAATGACCACCAGCCACGGTTTCCCAAAGGCGA  
GCAGGAGCTGGAAATCTCTGAGAGCGCTCTCTGCGAACCCGGATCCCCCTGGACAGAGCTC  
TTGACCCAGACACAGGCCCTAACACCCTGCACACCTACACTCTGTCTCCCAGTGAGCACTTT  
GCCTTGGATGTCAATTGTGGGCCCTGATGAGACCAACATGCAGAACTCATAGTGGTGAAGGA  
GCTGGACAGGGAAATCCATTCAATTTTTGATCTGGTGTAACTGCCTATGACAATGGGAACC  
CCCCAAGTCAGGTACCAAGCTTGGTCAAGGTCAACGTCTTGGACTCCAATGACAATAGCCCT  
GCGTTTGCTGAGAGTTCACTGGCACTGGAATCCAAGAAGATGCTGCACCTGGTACGCTTCT  
CATAAACTGACCGCCACAGACCCTGACCAAGGCCCAATGGGGAGGTGGAGTTCTTCTCA  
GTAAGCACATGCCTCCAGAGGTGCTGGACACCTTCAGTATTGATGCCAAGACAGGCCAGGTC  
ATTCTGCGTCGACCTCTAGACTATGAAAAGAACCTTGCCTACGAGGTGGATGTTCAAGCAAG  
GGACCTGGGTCCCAATCCTATCCAGCCCATTTGCAAGTTCTCATCAAGGTTCTGGATGTCA  
ATGACAACATCCCAAGCATCCACGTCACATGGGCCTCCAGCCATCACTGGTGTGAGAAGCT  
CTTCCCAAGGACAGTTTTATTGCTCTTGTGATGGCAGATGACTTGGATTGAGGACCAATGG  
TTTGGTCCACTGCTGGCTGAGCCAAGAGCTGGGCCACTTCAGGCTGAAAAGAACTAATGGCA  
ACACATACATGTTGCTAACCAATGCCCACTGGACAGAGAGCAGTGGCCCAAATATACCCCTC  
ACTCTGTTAGCCCAAGACCAAGGACTCCAGCCCTTATCAGCCAAGAAACAGCTCAGCATTCA  
GATCAGTGACATCAACGACAATGCACCTGTGTTTGAGAAAAGCAGGTATGAAGTCTCCACGC  
GGGAAAACAACCTTACCCTCTCTTACCTCATTACCATCAAGGCTCATGATGCAGACTTGGGC  
ATTAATGGAAAAGTCTCATACCGCATCCAGGACTCCCCAGTTGCTCACTTAGTAGCTATTGA  
CTCCAACACAGGAGAGGTCACTGCTCAGAGGTCACTGAACTATGAAGAGATGGCCGGCTTTG  
AGTTCCAGGTGATCGCAGAGGACAGCGGGCAACCCATGCTTGCATCCAGTGTCTGTGTGG  
GTCAGCCTCTTGGATGCCAATGATAATGCCCCAGAGGTGGTCCAGCCTGTGCTCAGCGATGG  
AAAAGCCAGCCTCTCCGTGCTTGTGAATGCCTCCACAGGCCACCTGCTGGTGCCCATCGAGA  
CTCCCAATGGCTTGGGCCAGCGGGCACTGACACACCTCCACTGGCCACTCACAGCTCCCGG  
CCATTCTTTTGACAACCATTTGTGGCAAGAGATGCAGACTCGGGGGCAAATGGAGAGCCCCCT  
CTACAGCATCCGCAATGGAAATGAAGCCACCTCTTCATCCTCAACCCTCATACGGGGCAGC  
TGTTGCTCAATGTACCAATGCCAGCAGCCTCATTGGGAGTGAGTGGGAGCTGGAGATAGTA  
GTAGAGGACCAGGGAAGCCCCCCTTACAGACCCGAGCCCTGTTGAGGGTCATGTTTGTGAC  
CAGTGTGGACCACCTGAGGGACTCAGCCCGCAAGCCTGGGGCCTTGAGCATGTGATGCTGA  
CGGTGATCTGCCTGGCTGTACTGTTGGGCATCTTCGGGTTGATCCTGGCTTTGTTTCATGTCC  
ATCTGCCGGACAGAAAAGAAGGACAACAGGGCCTACAACCTGTGGGAGGCGGAGTCCACCTA  
CCGCCAGCAGCCCAAGAGGCCCCAGAAACACATTGAGAAGGCAGACATCCACCTCGTGCCTG  
TGCTCAGGGGTGAGGAGGTGAGCCTTGTGAAGTCGGGCAGTCCCACAAAGATGTGGACAAG  
GAGGCGATGATGGAAGCAGGTGGGACCCCTGCCTGCAGGCCCCCTTCCACCTCACCCCGAC  
CCTGTACAGGACGCTGCGTAATCAAGGCAACCAGGGAGCACCGGCGGAGAGCCGAGAGGTGC  
TGCAAGACACGGTCAACCTCCTTTTCAACCATCCAGGCAGAGGAATGCCTCCCGGGAGAAC  
CTGAACCTTCCCGAGCCCCAGCCTGCCACAGGCCAGCCACGTTCCAGGCCTCTGAAGGTTGC  
AGGCAGCCCCACAGGGAGGCTGGCTGGAGACCAGGCGAGTGAGGAAGCCCCACAGAGGCCAC  
CAGCCTCCTCTGCAACCTGAGACGGCAGCGACATCTCAATGGCAAAGTGTCCCCTGAGAAA  
GAATCAGGGCCCCGTGAGATCCTGCGGAGCCTGGTCCGGCTGTCTGTGGCTGCCTTCGCCGA  
GCGGAACCCCGTGGAGGAGCTCACTGTGGATTCTCCTCCTGTTGAGCAAATCTCCAGCTGC  
TGTCTTGTGTCATCAGGGCCAATTCCAGCCCAAACCAACACCGAGGAAATAAGTACTTG  
GCCAAGCCAGGAGGCAGCAGGAGTGCAATCCAGACACAGATGGCCCAAGTGCAAGGGCTGG

**FIGURE 170B**

AGGCCAGACAGACCCAGAACAGGAGGAAGGGCCTTTGGATCCTGAAGAGGACCTCTCTGTGA  
AGCAACTGCTAGAGAAGAGCTGTCAAGTCTGCTGGACCCAGCACAGGTCTGGCCCTGGAC  
CGGCTGAGCGCCCTGACCCGGCCTGGATGGCGAGACTCTCTTTGCCCCCTACCACTA  
CCGTGACAATGTGATCTCCCCGGATGCTGCAGCCACGGAGGAGCCGAGGACCTTCCAGACGT  
TCGGCAAGGCAGAGGCACCAGAGCTGAGCCCAACAGGCACGAGGCTGGCCAGCACCTTTGTC  
TCGGAGATGAGCTCACTGCTGGAGATGCTGCTGGAACAGCGCTCCAGCATGCCCGTGGAGGC  
CGCCTCCGAGGCGCTGCGGCGGCTCTCGGTCTGCGGGAGGACCCTCAGTTTAGACTTGGCCA  
CCAGTGACGCCTCAGGCATGAAAGTGCAAGGGGACCCAGGTGGAAAGACGGGGACTGAGGGC  
AAGAGCAGAGGCAGCAGCAGCAGCAGCAGGTGCCTGTGAACATACCTCAGACGCCTCTGGAT  
CCAAGAACCAGGGGCCTGAGGATCTGTGGACAAGAGCTGGTTTCTAAAATCTTGTAACCTCAC  
TAGCTAGCGGCGGCCTGAGAACTTTAGGGTGACTGATGCTACCCCCACAGAGGAGGCAAGAG  
CCCCAGGACTAACAGCTGACTGACCAAGCAGCCCCTTGTAAGCAGCTCTGAGTCTTTTGGA  
GGACAGGGACGGTTTGTGGCTGAGATAAGTGTTCCTGGCAAAACATATGTGGAGCACAAAG  
GGTCAGTCCTCTGGCAGAACAGATGCCACGGAGTATCACAGGCAGGAAAGGGTGGCCTTCTT  
GGGTAGCAGGAGTCAGGGGGCTGTACCCTGGGGGTGCCAGGAAATGCTCTCTGACCTATCAA  
TAAAGGAAAAGCAGTAAAAAAAAAAAAAAAAAAAAA

**FIGURE 171**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA48331

<subunit 1 of 1, 1184 aa, 1 stop

<MW: 129022, pI: 5.20, NX(S/T): 5

MMQLLQLLLGLLGGPYLFLLGDCQEVTTTLTVKYQVSEEVPSGTVIGKLSQELGREERRRQA  
GAAFQVLQLPQALPIQVDSEEGLLSTGRRDLREQLCRQWDPCLVSFVDVLTATGDLALIHVEIQ  
VLDINDHQPRFPKGEQELEISESASLRTRIPDLRALDPDTGPNLTHTYTLSPSEHFALDVIV  
GPDETKHAELIVVKELDREIHSFFDLVLTAYDNGNPPKSGTSLVKVNVLDSDNDNSPAFAESS  
LALEIQEDAAPGTLTIKLTATDPDQGPNGEVEFFLSKHMPPEVLDTFSIDAKTGQVILRRPL  
DYEKNPAYEVDVQARDLGNPIPAHCKVLIKVLVDVNDNIPSIHVTWASQPSLVSEALPKDSF  
IALVMADDLDSGHNGLVHCWLSQELGHFRLKRTNGNTYMLLTNATLDREQWPKYTLTLLAQD  
QGLQPLSAKKQLSIQISDINDNAPVFEKSRYEVSTRENNLPSLHLITIKAHADLGINGKVS  
YRIQDSPVAHLVAIDSNTGEVTAQRSLNVEEMAGFEFQVIAEDSGQPMCLASSVSVWVSLDDA  
NDNAPEVVQPVLSDGKASLSVLVNASTGHLLVPIETPNGLGPAGTDTPLATHSSRPFLTT  
IVARDADSGANGEPLYSIRNGNEAHLFILNPHTGQLFVNVTNASSLIGSEWELEIVVEDQGS  
PPLQTRALLRVMFVTSVDHLRDSARKPGALSMSMLTVICLAVLLGIFGLILALFMSICRTEK  
KDNRAYNCREAESTYRQQPKRPQKHQKADIHLVPVLRGQAGEPCEVGQSHKDVKDKEAMMEA  
GWDPCLOAPFHLTPTLYRTLNRNQGNQGAPAESREVLQDTVNLLFNHPRQRNASRENLNLP  
QPATGQPRSRPLKVAGSPTGRLAGDQGSSEAPQRPASSATLRRQRHLNGKVSPEKESGPRQ  
ILRSLVRLSVAFAERNPVEELTVDSPPVQQISQLLSLLHQGQFQPKPNHRGNKYLAKEGGS  
RSAIPDTDGPSARAGGQTDPEQEEGPLDPEEDLSVKQLLEELSSLELDPSTGLALDRLSAPD  
PAWMARLSLPLTTNYRDNVISPDAAATEEPRTFQTFGKAEAPELSPTGTRLASTFVSEMSSL  
LEMLLEQRSSMPVEAASEALRRLSVCGRTLSLDLATSAAAGMKVQGDPPGKTGTGEGKSRGSS  
SSSRCL

**Important features:**

**Signal peptide:**

amino acids 1-13

**Transmembrane domain:**

amino acids 719-739

**N-glycosylation site.**

amino acids 415-418, 582-585, 659-662, 662-665 and 857-860

**Cadherins extracellular repeated domain signature.**

amino acids 123-133, 232-242, 340-350, 448-458 and 553-563

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**FIGURE 172**

CGGACGCGTGGGCGGACGCGTGGGGGAGAGCCGAGTCCCGGCTGCAGCACCTGGGAGAAGG  
CAGACCGTGTGAGGGGGCCTGTGGCCCCAGCGTGCTGTGGCCTCGGGGAGTGGGAAGTGGAG  
GCAGGAGCCTTCCTTACACTTCGCCATGAGTTTCCTCATCGACTCCAGCATCATGATTACCT  
CCCAGATACTATTTTTTGGATTGGGTGGCTTTTCTTCATGCGCCAATTGTTTAAAGACTAT  
GAGATACGTCAGTATGTTGTACAGGTGATCTTCTCCGTGACGTTTGCATTTTCTTGACCCAT  
GTTTGAGCTCATCATCTTTGAAATCTTAGGAGTATTGAATAGCAGCTCCCGTTATTTTCACT  
GGAAATGAACCTGTGTGTAATCTGCTGATCCTGGTTTTTCATGGTGCCTTTTACATTGGC  
TATTTTATTGTGAGCAATATCCGACTACTGCATAAACAACGACTGCTTTTTTCTGTCTCTT  
ATGGCTGACCTTTATGTATTTCTTCTGGAACTAGGAGATCCCTTTCCCATCTCAGCCCCAA  
AACATGGGATCTTATCCATAGAACAGCTCATCAGCCGGGTGGTGTGATTGGAGTGAATCTC  
ATGGCTCTTCTTTCTGGATTGGTGTGCTCAACTGCCCATACACTTACATGTCTTACTTCCT  
CAGGAATGTGACTGACACGGATATTCTAGCCCTGGAACGGCGACTGCTGCAAACCATGGATA  
TGATCATAAGCAAAAAGAAAAGGATGGCAATGGCACGGAGAACAATGTTCCAGAAGGGGGAA  
GTGCATAACAAACCATCAGGTTTCTGGGGAATGATAAAAAGTGTACCACCTCAGCATCAGG  
AAGTGAAGTCTTACTCTTATTCAACAGGAAGTGGATGCTTTGGAAGAATTAAGCAGGCAGC  
TTTTTCTGGAAACAGCTGATCTATATGCTACCAAGGAGAGAATAGAATACTCCAAAACCTTC  
AAGGGGAAATATTTTAATTTTCTTGTTACTTTTTCTCTATTTACTGTGTTTGGAAAATTT  
CATGGCTACCATCAATATTGTTTTTGATCGAGTTGGGAAAACGGATCCTGTCACAAGAGGCA  
TTGAGATCACTGTGAATTATCTGGGAATCCAATTTGATGTGAAGTTTTGGTCCCAACACATT  
CCCTTCATTCTTGTGGAATAATCATCGTCACATCCATCAGAGGATGCTGATCCTCTTAC  
CAAGTTCTTTTATGCCATCTCTAGCAGTAAGTCCCTCCAATGTCATTGTCCTGCTATTAGCAC  
AGATAATGGGCATGTACTTTGTCTCCTCTGTGCTGCTGATCCGAATGAGTATGCCTTTAGAA  
TACCGCACCATAATCACTGAAGTCCCTGGAGAACTGCAGTTCAACTTCTATCACCCTTGGTT  
TGATGTGATCTTCTGCTCAGCGCTCTCTCTAGCATACTCTTCTCTATTTGGCTCACAAAC  
AGGCACCAGAGAAGCAAATGGCACCTTGAAGTCAAGCTTCAAGCTGTTAGAGGCCAGT  
GGTTTCAAATTTAGATATAAGAGGGGGGAAAAATGGAACCAGGGCCTGACATTTTATAAAC  
AAACAAAATGCTATGGTAGCATTTTTTACCTTCATAGCATACTCCTTCCCCGTCAGGTGATA  
CTATGACCATGAGTAGCATCAGCCAGAACATGAGAGGGGAGAACTAACTCAAGACAATACTCA  
GCAGAGAGCATCCCGTGTGGATATGAGGCTGGTGTAGAGGCGGAGAGGAGCCAAGAACTAA  
AGGTGAAAAATACACTGGAAGTCTGGGGCAAGACATGTCTATGGTAGCTGAGCCAAACACGT  
AGGATTTCCGTTTTAAGGTTACATGGAAGGTTATAGCTTTGCCTTGAGATTGACTCATT  
AAAATCAGAGACTGTAACAAAAAAGGGCGGCCGCGACTCTAGAGTCG  
ACCTGCAGAAGCTTGGCCGCCATGGCCCAACTTGTTTATTGCAGCTTATAATG

**FIGURE 173**

MSFLIDSSIMITSQILFFGFGWLFFMRQLFKDYEIRQYVVQVIFSVTFASFCTMFELIIFEI  
LGVLNSSSRYPFHWMNLCVILLILVFMVPFYIGYFIVSNIRLLHKQRLLFSCLLWLTFMYFF  
WKLGDPPFPI LSPKHGILSIEQLISRVGVIGVTLMALLSGFGAVNCPYTYMSYFLRNVTDTDI  
LALERRLLQTMDMIISKKKRMAMARRTMFQKGEVHNKPSGFWGMIKSVTTSASGSENLTLIQ  
QEVDALEELSRQLFLETADLYATKERIEYSKTFKGKYFNFLGYFFSIYCVWKIFMATINIVE  
DRVGKTDVPVTRGIEITVNYLGIQFDVKFWSQHISFILVGIIIVTSIRGLLITLTKFFYAIS  
SKSSNVIVLLLAQIMGMYFVSSVLLIRMSMPLEYRTIITEVLGELQNFYHRWFEDVIFLVSA  
LSSILFLYLAHKQAPEKQMAP

**Important features:**

**Signal peptide:**

amino acids 1-23

**Potential transmembrane domains:**

amino acids 37-55, 81-102, 150-168, 288-311, 338-356, 375-398,  
425-444

**N-glycosylation sites.**

amino acids 67-70, 180-183 and 243-246

**Eukaryotic cobalamin-binding proteins**

amino acids 151-160

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**FIGURE 174**

CATGGGAAGTGGAGCCGGAGCCTTCCTTACACTCGCCATGAGTTTCCTCATCGACTCCAGCA  
TCATGATTACCTCCCNGANACTATTTTTTGGATTGGGTGGCTTTTCTTCNGCGCCAATGTT  
TAAAGACTATGAGATACGTCAGTATGTTGTACNGGTGATCTTCTCCGTGACGTTTGCCATT  
CTTGCACCATGTTTGAGCTCATCATCTTTGAAATCTTNGGAGTATTGAATAGCAGCTCCCGT  
TATTTTCACTGGAAAATGAACCTGTGTGTAATTCTGCTGATCCTGGTTNTCATGGTGCCTTT  
TTACATTGGCTATTTTATTGTGAGCAATATCCGACTACTGCATAACAACGACTGCTTTTTT  
CCTGTCTCTTATGGCTGACCTTTATGTATTTCCAG

**FIGURE 175**

GTGTTGCCCTTGGGGAGGGGAAGGGGAGCCNGGCCCTTTCCTAAAATTTGGCCAAGGGTTTC  
TTTNTTGAATTCCGGGTTNNGNATACCTTCCCAGAAAATATTTTTTGGATTGGGGTAGNTT  
TTTTTCATGCGCCAATTGTTTAAAGACTATGAGATACGTCAGTATGTTGTACAGGTGATNTT  
NTCCGTGACGTTTGCATTTTCTTGACCATGTTTGAGCTCATCATNTTGAATNTTAGGAG  
TATTGAATAGCAGCTCCCGTTATTTTCACTGGAAAATGAACCTGTGTGTAATTCTGCTGATC  
CTGGTTTTTCATGGTGCCTTTTACATTGGCTATTTTATTGTGAGCAATATCCGACTACTGCA  
TAAACAACGACTGCTTTTTTCCTGTCTNTTATGGCTGACCTTTATGTATTTNTTNTGGAAAN  
TAGGAGATCCCTTTCCCATTCCTC

**FIGURE 176A**

CTCGCGCAGGGATCGTCCCATGCGCGGGGCTCGGAGCCGCGACCCTTGGGGGGCCTCCGGGA  
TTTGCTACCTTTTTGGCTCCCTGCTCGTGAAGTCTCTTCTCACGGGCTGTGCGCTTCAAT  
CTGGACGTGATGGGTGCCTTGCAGCAAGGAGGGCGAGCCAGGCAGCCTCTTCGGCTTCTCTGT  
GGCCCTGCACCGGCAGTTGCAGCCCCGACCCAGAGCTGGCTGCTGGTGGGTGCTCCCCAGG  
CCCTGGCTCTTCTGCGGAGCAGGCGAATCGCACTGGAGGCCTCTTCGCTTGCCCGTTGAGC  
CTGGAGGAGACTGACTGCTACAGAGTGGACATCGACCAGGGAGCTGATATGAAAAGGAAAG  
CAAGGAGAACCAGTGGTTGGGAGTCAGTGTTCGGAGCCAGGGGCTGGGGGCAAGATTGTTA  
CCTGTGCACACCGATATGAGGCAAGGCAGCGAGTGGACCAGATCCTGGAGACGCGGGATATG  
ATTGGTCGCTGCTTTGTGCTCAGCCAGGACCTGGCCATCCGGGATGAGTTGGATGGTGGGA  
ATGGAAGTTCTGTGAGGGACGCCCCAAGGCCATGAACAATTTGGGTTCTGCCAGCAGGGCA  
CAGCTGCCGCCTTCTCCCTGATAGCCACTACCTCCTCTTTGGGGCCCCAGGAACCTATAAT  
TGGAAGGGCACGGCCAGGGTGGAGCTCTGTGCACAGGGCTCAGCGGACCTGGCACACCTGGA  
CGACGGTCCCTACGAGGCGGGGGGAGAGAAGGAGCAGGACCCCCGCCTCATCCCGGTCCCTG  
CCAACAGCTACTTTGGCTTCTCTATTGACTCGGGGAAAGGTCTGGTGCGTGCAGAAGAGCTG  
AGCTTTGTGGCTGGAGCCCCCGCGCCAACCACAAGGGTGTGTGGTTCATCCTGCGCAAGGA  
CAGCGCCAGTCGCTGGTGGCGAGGTTATGCTGTCTGGGGAGCGCCTGACCTCCGGCTTTG  
GCTACTCACTGGCTGTGGCTGACCTCAACAGTGTGGCTGGCCAGACCTGATAGTGGGTGCC  
CCCTACTCTTTTGAAGCGCAAGAAGAGCTGGGGGGTGTGTGTATGTGTACTTGAACCAGGG  
GGGTCACTGGGCTGGGATCTCCCTCTCCGGCTCTGCGGCTCCCTGACTCCATGTTTCGGGA  
TCAGCCTGGCTGTCTGGGAGACCTCAACCAAGATGGCTTCCAGATATTGCAGTGGGTGCC  
CCCTTTGATGGTGTATGGGAAAGTCTTCACTACCATGGGAGCAGCCTGGGGGTTGTGCCAA  
ACCTTCACAGGTGCTGGAGGGCGAGGCTGTGGGCATCAAGAGCTTCGGCTACTCCCTGTGAG  
GCAGCTTGGATATGGATGGGAACCAATACCTGACCTGCTGGTGGGCTCCCTGGCTGACACC  
GCAGTGCTCTTCAGGGCCAGACCCATCCTCCATGTCTCCCATGAGGTCTCTATTGTCTCCAG  
AAGCATCGACCTGGAGCAGCCCAACTGTGCTGGCGGCCACTCGGTCTGTGTGGACCTAAGGG  
TCTGTTTTAGCTACATTGCAGTCCCCAGCAGCTATAGCCCTACTGTGGCCCTGGACTATGTG  
TTAGATGCGGACACAGACCGGAGGCTCCGGGGCCAGGTTCCCCGTGTGACGTTCTTGAGCCG  
TAACCTGGAAGAACCACAGCACCAGGCCTCGGGCACCCTGTGGCTGAAGCACCAGCATGACC  
GAGTCTGTGGAGACGCCATGTTCCAGCTCCAGGAAATGTCAAAGACAAGCTTCGGGCTATT  
GTAGTGACCTTGTCTACAGTCTCCAGACCCCTCGGCTCCGGCGACAGGCTCCTGGCCAGGG  
GCTGCCTCCAGTGGCCCCCATCCTCAATGCCACCAGCCAGCACCAGCGGGCAGAGATCC  
ACTTCCTGAAGCAAGGCTGTGGTGAAGACAAGATCTGCCAGAGCAATCTGCAGCTGGTCCAC  
GCCCCGCTTCTGTACCCGGGTGAGCGACACGGAATTCCAACCTCTGCCCATGGATGTGGATGG  
AACAACAGCCCTGTTTGCACTGAGTGGGCAGCCAGTCATTGGCCTGGAGCTGATGGTCACCA  
ACCTGCCATCGGACCCAGCCAGCCCGAGGCTGATGGGGATGATGCCCATGAAGCCAGCTC  
CTGGTCATGCTTCTGACTCACTGCACTACTCAGGGGTCCGGGCTTGGACCCTGCGGAGAA  
GCCACTCTGCCTGTCCAATGAGAATGCCTCCCATGTTGAGTGTGAGCTGGGGAACCCCATGA  
AGAGAGGTGCCAGGTACCTTCTACCTCATCCTTAGCACCTCCGGGATCAGCATTGAGACC  
ACGGAAGTGGAGGTAGAGCTGCTGTTGGCCACGATCAGTGAGCAGGAGCTGCATCCAGTCTC  
TGCACGAGCCCGTGTCTTATTGAGCTGCCACTGTCCATTGCAGGAATGGCCATTCCCCAGC  
AATCTTCTTCTCTGGTGTGGTGAAGGGCGAGAGGCCATGCAGTCTGAGCGGGATGTGGGC  
AGCAAGGTCAAGTATGAGGTACGGTTTCCAACCAAGGCCAGTCGCTCAGAACCCTGGGCTC  
TGCTTCTTCAACATCATGTGGCCTCATGAGATTGCCAATGGGAAGTGGTTGCTGTACCCAA  
TGCAAGTTGAGCTGGAGGGCGGGCAGGGGCTGGGCAGAAAGGGCTTTGCTCTCCAGGGCC  
AACATCCTCCACCTGGATGTGGACAGTAGGGATAGGAGGCGGCGGGAGCTGGAGCCACCTGA  
GCAGCAGGAGCCTGGTGAGCGGCAGGAGCCAGCATGTCTGTTGGTGGCAGTGTCTCTGCTG  
AGAAGAAGAAAACATCACCCTGGACTGCGCCCGGGGCACGGCCAACCTGTGTGGTGTTCAGC  
TGCCCACTCTACAGCTTTGACCGCGGGCTGTGCTGCATGTCTGGGGCCGTCTCTGGAACAG  
CACCTTTCTGGAGGAGTACTCAGCTGTGAAGTCCCTGGAAGTGATTGTCCGGGCCAACATCA  
CAGTGAAGTCCCTCCATAAAGAACTTGATGCTCCGAGATGCCTCCACAGTGATCCCACTGATG  
GTATACTTGGACCCCATGGCTGTGGTGGCAGAAGGAGTGCCCTGGTGGGTATCCTCCTGGC  
TGTAAGTGGCTGGGCTGCTGGTGTGCTAGCACTGCTGGTGTGCTCCTGTGGAAGATGGGATTCT  
TCAAACGGGGCGAAGCACCCTGAGGCCACCGTGCCCCAGTACCATGCGGTGAAGATTCTCGG  
GAAGACCGACAGCAGTTCAAGGAGGAGAAGACGGGCACCATCCTGAGGAACAACCTGGGGCAG



**FIGURE 176B**

CCCCGGCGGGAGGGCCCGGATGCACACCCCATCCTGGCTGCTGACGGGCATCCCGAGCTGG  
GCCCCGATGGGCATCCAGGGCCAGGCACCGCCTAGGTTCCCATGTCCCAGCCTGGCCTGTGG  
CTGCCCTCCATCCCTTCCCCAGAGATGGCTCCTTGGGATGAAGAGGGTAGAGTGGGCTGCTG  
GTGTCGCATCAAGATTGGCAGGATCGGCTTCCTCAGGGGCACAGACCTCTCCACCCACAA  
GAACTCCTCCACCCAACCTTCCCCTTAGAGTGCTGTGAGATGAGAGTGGGTAAATCAGGGAC  
AGGGCCATGGGGTAGGGTGAGAAGGGCAGGGGTGTCCTGATGCAAAGGTGGGGAGAAGGGAT  
CCTAATCCCTTCCTCTCCCATTCACCCTGTGTAACAGGACCCCAAGGACCTGCCTCCCCGGA  
AGTGCCTTAACCTAGAGGGTCGGGGAGGAGGTTGTGTCACTGACTCAGGCTGCTCCTTCTCT  
AGTTTCCCCTCTCATCTGACCTTAGTTTGCTGCCATCAGTCTAGTGGTTTCGTGGTTTCGTC  
TATTTATTAAAAATATTTGAGAACAAAAAAAAAAAAAAAAAAAA

**FIGURE 177**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA55737

><subunit 1 of 1, 1141 aa, 1 stop

><MW: 124671, pI: 5.82, NX(S/T): 5

MAGARSRDPWGASGICYLFGSLLVELLFSRAVAFNLDVMGALRKEGEPGSLFGFSVALHRQL  
QPRPQSWLLVGAPQALALPGQQANRTGGLFACPLSLEETDCYRVDIDQGADMOKESKENQWL  
GVSVRSQGGPGKIVTCAHRYEARQRVDQILETRDMIGRCFVLSQDLAIRDELDDGGWKFCG  
RPOGHEQFGFCQQGTAAAFSPDSHYLLFGAPGTYNWKGRTARVELCAQGSADLAHLDDGPYEA  
GGEKEQDPRLIPVPANSYFGFSIDSGKGLVRAEELS FVAGAPRANHKGAVVILRKDSASRLV  
PEVMLSGERLTSGFGYSLAVADLNSDGWPD LIVGAPYFFERQEELGGAVYVYLNQGGHWAGI  
SPLRLCGSPDSMFGISLAVLGDNLQDGFPIAVGAPFDGDGKVFIYHGSSLGVVAKPSQVLE  
GEAVGIKSFYSLSGSLDMDGNQYPDLLVGLADTAVLFRARPILHVSHEVSIAPRSIDLEQ  
PNCAGGHSVCVDLRVCFSYIAVPSSYSPTVALDYVLDADTDRLRGQVPRVTFLSRNLEPK  
HQASGTVWLKHQHDRVCGDAMFQLQENVKDKLRAIVVTLSSYSLQTPRLRRQAPGQGLPPVAP  
ILNAHQ PSTQRAEIHFLKQGCCGEDKICQSNLQLVHARFCTRVSDTEFQPLPMDVDGTTALFA  
LSGQPVIGLELMVTNLPSDPAQPADGDDAHEAQLLVMLPDSLHYSGVRLDPAEKPLCLSN  
ENASHVECELGNPMKRG AQVTFFYLILSTSGISIIETTELEVLLIATISEQELHPVSARARVF  
IELPLSIAGMAIPQQLFFSGVVRGERAMQSERDVGSKVKEYEVTVSNOGQSLRTLGS AFLNIM  
WPHEIANGKWL LYPMQVELEGGQGPQKGLCSRPNHLHLDVDSRDRRRRELEPPEQQEPGE  
RQEPSMSWWPVSSAEKKKNITLDCARGTANCVVFSCPLYSFDRAAVLHVWGRLWNSTFLEEY  
SAVKSLEIVRANITVKSSIKNLMLRDASTVIPVMVYLDPMVVAEGVPWWVILLAVLAGLL  
VLALLVLLLWKMGFFKRAKHPEATVPQYHAVKIPREDRQQFKEEKTGTILRNNWGS PRREGP  
DAHPIAADGHPGLGPDGHPGPGTA

**Important features:**

**Signal peptide:**

amino acids 1-33

**Transmembrane domain:**

amino acids 1039-1064

**N-glycosylation sites.**

amino acids 86-89, 746-749, 949-952, 985-988 and 1005-1008

**Integrins alpha chain proteins.**

amino acids 1064-1071, 384-408, 1041-1071, 317-346, 443-465, 385-407, 215-224, 634-647, 85-99, 322-346, 470-479, 442-466, 379-408 and 1031-1047

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**FIGURE 178**

CGCGCCGGGCGCAGGGAGCTGAGTGGACGGCTCGAGACGGCGGCGCGTGCAGCAGCTCCAGA  
AAGCAGCGAGTTGGCAGAGCAGGGCTGCATTTCCAGCAGGAGCTGCGAGCACAGTGCTGGCT  
CACAACAAGATGCTCAAGGTGTCAGCCGTACTGTGTGTGTGTGCAGCCGCTTGTTGTCAGTCA  
GTCTCTCGCAGCTGCCGCGGCGGTGGCTGCAGCCGGGGGGCGGTTCGACGGCGGTAATTTTC  
TGGATGATAAACAATGGCTCACCACAATCTCTCAGTATGACAAGGAAGTCGGACAGTGGAAC  
AAATTCCGAGACGAAGTAGAGGATGATTATTTCCGCACCTTGAGTCCAGGAAAACCTTCGA  
TCAGGCTTTAGATCCAGCTAAGGATCCATGCTTAAAGATGAAATGTAGTCGCCATAAAGTAT  
GCATTGCTCAAGATTCTCAGACTGCAGTCTGCATTAGTCACCGGAGGCTTACACACAGGATG  
AAAGAAGCAGGAGTAGACCATAGGCAGTGGAGGGTCCCATATTATCCACCTGCAAGCAGTG  
CCCAGTGGTCTATCCCAGCCCTGTTTGTGGTTCAGATGGTCATACCTACTCTTTTCAGTGCA  
AACTAGAATATCAGGCATGTGTCTTAGGAAAACAGATCTCAGTCAAATGTGAAGGACATTGC  
CCATGTCCTTCAGATAAGCCCACCAGTACAAGCAGAAATGTTAAGAGAGCATGCAGTGACCT  
GGAGTTCAGGGAAGTGGCAAACAGATTGCGGGACTGGTTCAGGCCCTTCATGAAAGTGGAA  
GTCAAAACAAGAAGACAAAACATTGCTGAGGCCTGAGAGAAGCAGATTGATACCAGCATC  
TTGCCAATTTGCAAGGACTCACTTGGCTGGATGTTTAAACAGACTTGATACAACTATGACCT  
GCTATTGGACCAGTCAGAGCTCAGAAGCATTACCTTGATAAGAATGAACAGTGTACCAAGG  
CATTCTTCAATTCTTGTGACACATACAAGGACAGTTAATATCTAATAATGAGTGGTGCTAC  
TGCTTCCAGAGACAGCAAGACCCACCTTGCCAGACTGAGCTCAGCAATATTCAGAAGCGGCA  
AGGGGTAAAGAAGCTCCTAGGACAGTATATCCCCCTGTGTGATGAAGATGGTTACTACAAGC  
CAACACAATGTCATGGCAGTGTGGACAGTGCTGGTGTGTGACAGATATGGAAATGAAGTC  
ATGGGATCCAGAATAAATGGTGTTCAGATTGTGCTATAGATTTTGAGATCTCCGGAGATTT  
TGCTAGTGGCGATTTTCATGAATGGACTGATGATGAGGATGATGAAGACGATATTATGAATG  
ATGAAGATGAAATTGAAGATGATGATGAAGATGAAGGGGATGATGATGATGGTGGTGTATGAC  
CATGATGTATACATTTGATTGATGACAGTTGAAATCAATAAATTCTACATTTCTAATATTTA  
CAAAAATGATAGCCTATTTAAAATTATCTTCTTCCCCAATAACAAAATGATTCTAAACCTCA  
CATATATTTTGTATAATTATTTGAAAAATTGCAGCTAAAGTTATAGAACTTTATGTTTAAAT  
AAGAATCATTTGCTTTGAGTTTTTATATTCCTTACACAAAAGAAAATACATATGCAGTCTA  
GTCAGACAAAATAAAGTTTTGAAGTGCTACTATAATAAATTTTTTACGAGAACAACTTTGT  
AAATCTTCCATAAGCAAAATGACAGCTAGTGCTTGGGATCGTACATGTTAATTTTTTGAAG  
ATAATTCTAAGTGAAATTTAAAATAAATAAATTTTTAATGACCTGGGTCTTAAGGATTTAGG  
AAAAATATGCATGCTTTAATTGCATTTCCAAAGTAGCATCTTGCTAGACCTAGATGAGTCAG  
GATAACAGAGAGATACCACATGACTCCAAAAA

**FIGURE 179**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA49829

><subunit 1 of 1, 436 aa, 1 stop

><MW: 49429, pI: 4.80, NX(S/T): 0

MLKVSAVLCVCAAAWCSQSLAAAAVAAAGGRSDGGNFLDDKQWLTTISQYDKEVGQWNKFR  
DEVEDDYFRTWSPGKPFQALDPAKDPCLMKCSRHKVCIAQDSQTAVCISHRRLTHRMKEA  
GVDHRQWRGPILSTCKQCPVVYPSPVCGSDGHTYSFQCKLEYQACVLGKQISVKCEGHCPCP  
SDKPTSTSRNVKRACSDLEFREVANRLRDWFKALHESGSQNKKTLLRPERSRFDTSILPI  
CKDSLGMFMNRLDTNYDLLLDQSELRSIYLDKNEQCTKAFFNSCDTYKDSLISNNEWCYCFQ  
RQODPPCQTELSNIQKRQGVKKLLGQYIPLCEDGYYKPTQCHGSVGQCWCVDYRGNEVMGS  
RINGVADCAIDFEISGDFASGDFHEWTDEDEDEDDIMNDEDEIEDDDEDEGDDDDGGDDHDVYI

**Important features:**

**Signal peptide:**

amino acids 1-16

**Leucine zipper pattern.**

amino acids 246-267

**N-myristoylation sites.**

amino acids 357-362, 371-376 and 376-381

**Thyroglobulin type-1 repeat proteins**

amino acids 353-365 and 339-352

**FIGURE 180A**

CAGACTCCAGATTTCCCTGTCAACCACGAGGAGTCCAGAGAGGAAACGCGGAGCGGAGACAA  
CAGTACCTGACGCCTCTTTTCAGCCCCGGGATCGCCCCAGCAGGGATGGGCGACAAGATCTGGC  
TGCCCTTCCCCGTGCTCCTTCTGGCCGCTCTGCCTCCGGTGCTGCTGCCTGGGGCGGCCGGC  
TTCACACCTTCCCTCGATAGCGACTTCACCTTTACCCTTCCCGCCGCCAGAAGGAGTGCTT  
CTACCAGCCCATGCCCCCTGAAGGCCTCGCTGGAGATCGAGTACCAAGTTTTAGATGGAGCAG  
GATTAGATATTGATTTCCATCTTGCTCTCCAGAAGGCAAAACCTTAGTTTTTGAACAAAGA  
AAATCAGATGGAGTTCACACTGTAGAGACTGAAGTTGGTGATTACATGTTCTGCTTTGACAA  
TACATTACAGCACCATTCTGAGAAGGTGATTTTCTTTGAATTAATCCTGGATAATATGGGAG  
AACAGGCACAAGAACAAGAAGATTGGAAGAAATATATTACTGGCACAGATATATTGGATATG  
AAACTGGAAGACATCCTGGAATCCATCAACAGCATCAAGTCCAGACTAAGCAAAAGTGGGCA  
CATACAAATTCTGCTTAGAGCATTGGAAGCTCGTGATCGAAACATACAAGAAAGCAACTTTG  
ATAGAGTCAATTTCTGGTCTATGGTTAATTTAGTGGTCATGGTGGTGGTGTGAGCCATTCAA  
GTTTATATGCTGAAGAGTCTGTTTGAAGATAAGAGGAAAAGTAGAACTTAAAACTCCAACT  
AGAGTACGTAACATTGAAAAATGAGGCATAAAATGCAATAAACTGTTACAGTCAAGACCAT  
TAATGGTCTTCTCCAAAATATTTTGAGATATAAAAGTAGGAAACAGGTATAATTTAATGTG  
AAAATTAAGTCTTCACTTTCTGTGCAAGTAATCCTGCTGATCCAGTTGTACTTAAGTGTGTA  
ACAGGAATATTTGCGAATATAGGTTAACTGAATGAAGCCATATTAATAACTGCATTTTC  
CTAACTTTGAAAAATTTTGCAATGTCTTAGGTGATTTAAATAAATGAGTATTGGGCCTAAT  
TGCAACACCAGTCTGTTTTAACAGGTTCTATTACCCAGAACTTTTTTGTAATGCGGCAGT  
TACAAATTAAGTGTGGAAGTTTTAGTTTAAAGTTATAAATCACCTGAGAATTACCTAATGA  
TGGATTGAATAAATCTTTAGACTACAAAAGCCCAACTTTCTCTATTACATATGCATCTCT  
CCTATAATGTAAATAGAATAATAGCTTTGAAATACAATTAGGTTTTTGAGATTTTATAACC  
AAATACATTTTCACTGTAAACATATTAGCAGAAAGCATTAGTCTTTGTACTTTGCTTACATTCC  
CAAAAGCTGACATTTTACGATTCTTAAAAACACAAAGTTACACTTACTAAATTAGGACAT  
GTTTTCTCTTTGAAATGAAGAATATAGTTTAAAGCTTCTCCTCCATAGGGACACATTTTC  
TCTAACCTTAACTAAAGTGATGATTTTAAATTAATGTGAGGTAAAATAAGTTTATTTT  
TAATAGTATCTGTCAAGTTAATATCTGTCAACAGTTAATAATCATGTTATGTTAATTTTAAC  
ATGATTGCTGACTTGGATAATTCATTATTACCAGCAGTTATGAAGGAAATATTGCTAATG  
ATCTGGGCCTACCATAAATAAATATCTCCTTTCTGAGCTCTAAGAATTATCAGAAACAGG  
AAAGAATTTAGAAAACTTGAGAAAACCTAATCCAAAATAAATTCACTTAAGTAGAATAT  
AAATAAATATCTAGAATCTGACTGGCTCATCATGACATCCTACTCATAACATAAATCAAAGG  
AGATGATTAATTTCCAGTTAGCTGGAAGAACTTTGGCTGTAGGTTTTTATTTTCTACAAGA  
ATTCTGGTTTTGAATTATTTTTGTAAGCAGGTACATTTTATAAAATGTAAGCCCTACTGTAAG  
GTTTAGCACTGGGTGTACATATTTATTAATAATTTTTATTATAACAATTTTATTAATAATGG  
CCTTTCTGAACACTTTATTTATTGATGTTGAAGTAAGGATTAGAAACATAGACTCCCAAGTT  
TTAAACACCTAAATGTGAATAACCCATATATACAACAAAGTTTCTGCCATCTAGCTTTTTGA  
AGTCTATGGGGTCTTACTCAAGTACTAGTAATTTAACTTCATCATGAATGAATATAATTT  
TTAAGTTATGCCATTTATAACGTTGTTTATGACTACATTGTGAGTTAGAAACAACTTAA  
ATTTGGGGTATAGAACCCCTCAACAGGTTAGTAATGCTGGAATTCTTGATGAGCAATAATGA  
TAACCAGAGAGTGATTTTCACTCATAGTAGTATAAAAAGAGATACATTTCCCTCTTA  
GGCCCTGGGAGAAGAGCAGCTTAGATTTCCCTACTGGCAAGGTTTTTAAAAATGAGGTAA  
TGCCGTATATGATCAATTACCTTAATTGGCCAAGAAATGCTTCAGGTGTCTAGGGGTATCC  
TCTGCAACACTTGCGAACAAGGTCAATAAGATCCTTGCCATGAATACCCCTCCCTTTTG  
CGCTGTTAAATTTGCAATGAGAAGCAAATTTACAGTACCATAACTAATAAAGCAGGGTACAG  
ATATAAACTACTGCATCTTTCTATAAACTGTGATTAAAGAATTCTACCTCTCCTGTATGGC  
TGTTACTGTACTGTACTCTGACTCCTTACCTAACAAATGAATTTGTTACATAATCTTCTAC  
ATGTATGATTTGTGCCACTGATCTTAAACCTATGATTAGTAACTTCTTACCATATAAAAAC  
GATAATTGCTTTATTTGGAAAAGAATTAGGAATACCTAAGGACAATTATTTTATAGACAAA  
GTAAAAAGACAGATATTTAAGAGGCATAACCAAAAAGCAAACTTGTAACAGAGTAAAA  
TCTTTAATATTTCTAAAGACATACTGTTTATCTGCTTCATATGCTTTTTTTAATTTCACTAT  
TCCATTTCTAAATTAAGTTATGCTAAATGAGTAAGCTGTTTATCACTTAACAGCTCATTT  
TGTCTTTTTCAATATACAAATTTTAAAAATACTACAATATTTAACTAAGGCCCAACCGATTT  
CCATAATGTAGCAGTTACCGTGTTACCTCACACTAAGGCCTAGAGTTTGCTCTGATATGCA  
TTTGGATGATTAATGTTATGCTGTTCTTTCATGTGAATGTCAAGACATGGAGGGTGTGTA

**FIGURE 180B**

ATTTTATGGTAAAATTAATCCTTCTTACACATAATGGTGTCTTAAAATTGACAAAAAATGAG  
CACTTACAATTGTATGTCTCCTCAAATGAAGATTCTTTATGTGAAATTTTAAAAGACATTGA  
TTCCGCATGTAAGGATTTTTCATCTGAAGTACAATAATGCACAATCAGTGTTGCTCAAACCTG  
CTTTATACTTATAAACAGCCATCTTAAATAAGCAACGTATTGTGAGTACTGATATGTATATA  
ATAAAAATTATCAAAGGAAAA

**FIGURE 181**

></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA52196

><subunit 1 of 1, 229 aa, 1 stop

><MW: 26017, pI: 4.73, NX(S/T): 0

MGDKIWLPPFPVLLLAALPPVLLPGAAGFTPSLSDFTFTLPAGQKECFYQPMPLKASLEIEY  
QVLGDGAGLDIDFHLASPEGKTLVFEQRKSDGVHTVETEVDYMFCDNTFSTISEKVIFFEEL  
ILDNMGEQAQEQEDWKYITGTDILDMKLEDILESINSIKSRLSKSGHIQILLRAFEARDRN  
IQESNFDVRVNFWSMVNLVVMVVSAIQVYMLKSLFEDKRKSRT

**Important features:**

**Signal peptide:**

amino acids 1-23

**Transmembrane domain:**

amino acids 195-217

**N-myristoylation site.**

amino acids 43-48

**Tyrosine kinase phosphorylation site.**

amino acids 55-62

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**FIGURE 182**

CCATCCCTGAGATCTTTTTATAAAAAACCCAGTCTTTGCTGACCAGACAAAGCATACCAGAT  
CTCACCAGAGAGTCGCAGACACTATGCTGCCTCCCATGGCCCTGCCCAGTGTGTCCTGGATG  
CTGCTTTCCTGCCTCATTCTCCTGTGTCAGGTTCAAGGTGAAGAAACCCAGAAGGAACTGCC  
CTCTCCACGGATCAGCTGTCCCAAAGGCTCCAAGGCCTATGGCTCCCCCTGCTATGCCTTGT  
TTTTGTCAACAAAATCCTGGATGGATGCAGATCTGGCTTGCCAGAAGCGGCCCTCTGGAAAA  
CTGGTGTCTGTGCTCAGTGGGGCTGAGGGATCCTTCGTGTCCTCCCTGGTGAGGAGCATTAG  
TAACAGCTACTCATACATCTGGATTGGGCTCCATGACCCACACAGGGCTCTGAGCCTGATG  
GAGATGGATGGGAGTGGAGTAGCACTGATGTGATGAATTACTTTGCATGGGAGAAAAATCCC  
TCCACCATCTTAAACCCTGGCCACTGTGGGAGCCTGTCAAGAAGCACAGGATTTCTGAAGTG  
GAAAGATTATAACTGTGATGCAAAGTTACCCTATGTCTGCAAGTTCAAGGACTAGGGCAGGT  
GGGAAGTCAGCAGCCTCAGCTTGGCGTGCAGCTCATCATGGACATGAGACCAGTGTGAAGAC  
TCACCCTGGAAGAGAATATTCTCCCCAACTGCCCTACCTGACTACCTTGTCATGATCCTCC  
TTCTTTTTTCCTTTTTCTTCACCTTCATTTAGGCTTTTCTCTGTCTTCCATGTCTTGAGATC  
TCAGAGAATAATAATAAAATGTTACTTTATAAAAAAAAAAAAAAAAAAAAAA



**FIGURE 183**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56965

<subunit 1 of 1, 175 aa, 1 stop

<MW: 19330, pI: 7.25, NX(S/T): 1

MLPPMALPSVSWMLLSCLILLCQVQGEETQKELPSPRISCPKGSKAYGSPCYALFLSPKSWM  
DADLACQKRPSGKLVSVLGAEGSFVSSLVRSISNSYSYIWIGLHDPTQGSEPDGDGWEWSS  
TDVMNYFAWEKNPSTILNPGHCGSLSRSTGFLKWKDYNCDAKLPYVCKFKD

Important features:

Signal peptide:

amino acids 1-26

C-type lectin domain signature.

amino acids 146-171

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**FIGURE 184**

CCAGTCTGTCGCCACCTCACTTGGTGTCTGCTGTCCCCGCCAGGCAAGCCTGGGGTGAGAGC  
ACAGAGGAGTGGGCCGGGACCATGCGGGGGACGCGGCTGGCGCTCCTGGCGCTGGTGCTGGC  
TGCTTGCGGAGAGCTGGCGCCGGCCCTGCGCTGCTACGTCTGTCCGGAGCCCACAGGAGTGT  
CGGACTGTGTCACCATCGCCACCTGCACCACCAACGAAACCATGTGCAAGACCACACTCTAC  
TCCCGGGAGATAGTGTACCCCTTCCAGGGGGACTCCACGGTGACCAAGTCCTGTGCCAGCAA  
GTGTAAGCCCTCGGATGTGGATGGCATCGGCCAGACCCTGCCCCTGCTCCTGTGCAATACTG  
AGCTGTGCAATGTAGACGGGGCGCCCGCTCTGAACAGCCTCCACTGCGGGGCCCTCACGCTC  
CTCCCACTCTTGAGCCTCCGACTGTAGAGTCCCCGCCACCCCATGGCCCTATGCGGCCCA  
GCCCCGAATGCCTTGAAGAAGTGCCCCCTGCACCAGGAAAAAAAAAAAAAAAAA

**FIGURE 185**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56405

<subunit 1 of 1, 125 aa, 1 stop

<MW: 13115, pI: 5.90, NX(S/T): 1

MRGTRLALLALVLAACGELAPALRCYVCPEPTGVSDCVTIATCTTNETMCKTTLYSREIVYP  
FQGDSTVTKSCASKCKPSDVDGIGQTLVPVSCCNTELCNVDGAPALNSLHCGALTLLPLLSRL

**Important features:**

**Signal peptide:**

amino acids 1-17

**N-glycosylation site.**

amino acids 46-49

**FIGURE 186**

CTGCAGTCAGGACTCTGGGACCGCAGGGGGCTCCCGGACCCCTGACTCTGCAGCCGAACCGGC  
ACGGTTTCGTGGGGACCCAGGCTTGCAAAGTGACGGTCATTTTCTCTTTCTTTCTCCCTCTT  
GAGTCCTTCTGAGATGATGGCTCTGGGCGCAGCGGGAGCTACCCGGGTCTTTGTGCGGATGG  
TAGCGGGCGGCTCTCGGCGGCCACCCCTCTGCTGGGAGTGAGCGCCACCTTGAACCTCGGTTCTC  
AATTCCAACGCTATCAAGAACCTGCCCCACCGCTGGGCGGCGCTGCGGGGCACCCAGGCTC  
TGCAGTCAGCGCCGCGCCGGGAATCCTGTACCCGGGCGGGAATAAGTACCAGACCATTGACA  
ACTACCAGCCGTACCCGTGCGCAGAGGACGAGGAGTGCGGCACCTGATGAGTACTGCGCTAGT  
CCCACCCGCGGAGGGGACGCAGGCGTGCAAATCTGTCTCGCCTGCAGGAAGCGCCGAAAACG  
CTGCATGCGTCACGCTATGTGCTGCCCCGGGAATTACTGCAAAAATGGAATATGTGTGTCTT  
CTGATCAAAATCATTTCGAGGAGAAATTGAGGAAACCATCACTGAAAGCTTTGGTAATGAT  
CATAGCACCTTGGATGGGTATTCCAGAAGAACCACCTTGTCTTCAAAAATGTATCACACCAA  
AGGACAAGAAGGTTCTGTTTGTCTCCGGTCATCAGACTGTGCCTCAGGATTGTGTTGTGCTA  
GACACTTCTGGTCCAAGATCTGTAAACCTGTCCTGAAAGAAGGTCAAGTGTGTACCAAGCAT  
AGGAGAAAAGGCTCTCATGGACTAGAAATATTCCAGCGTTGTTACTGTGGAGAAGGTCTGTC  
TTGCCGGATACAGAAAGATCACCATCAAGCCAGTAATTCTTCTAGGCTTCACACTTGTGAGA  
GACACTAAACCAGCTATCCAAATGCAGTGAACCTCTTTTATATAATAGATGCTATGAAAACC  
TTTTATGACCTTCATCAACTCAATCCTAAGGATATACAAGTTCTGTGGTTTCAGTTAAGCAT  
TCCAATAACACCTTCCAAAAACCTGGAGTGTAAGAGCTTTGTTTCTTTATGGAACCTCCCCTG  
TGATTGCAGTAAATTACTGTATTGTAAATTCTCAGTGTGGCACTTACCTGTAAATGCAATGA  
AACTTTTAATTATTTTTCTAAAGGTGCTGCACTGCCATTTTTCTCTTTGTATGTAAATTT  
TTGTACACATTGATTGTTATCTTGACTGACAAATATTCTATATTGAACTGAAGTAAATCATT  
TCAGCTTATAGTTCTTAAAAGCATAACCCCTTACCCCATTTAATTCTAGAGTCTAGAACGCA  
AGGATCTCTTGGAATGACAAATGATAGGTACCTAAAATGTAAACATGAAAATACTAGCTTATT  
TTCTGAAATGTACTATCTTAATGCTTAAATTATATTCCCTTTAGGCTGTGATAGTTTTTTGA  
AATAAAATTTAACATTTAAAAA

**FIGURE 187**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA57530

<subunit 1 of 1, 266 aa, 1 stop

<MW: 28672, pI: 8.85, NX(S/T): 1

MMALGAAGATRVFVAMVAAALGGHPLLGVSATLNSVLNSNAIKNLPPPLGGAAGHPGSAVSA  
APGILYPGGNKYQTIIDNYQPYPCAEDEECGTDEYCASPTRGGDAGVQICLACRKRRCMRH  
AMCCPGNYCKNGICVSSDQNHFRGEIEETITESFGNDHSTLDGYSRRTTLSSKMYHTKGQEG  
SVCLRSSDCASGLCCARHFWSKICKPVLKEGQVCTKHRRKGSHGLEIFQRCYCGEGLSCRIQ  
KDHHQASNSSRLHTCQRH

**Important features:**

**Signal peptide:**

amino acids 1-23

**N-glycosylation site.**

amino acids 256-259

**Fungal Zn(2)-Cys(6) binuclear cluster domain**

amino acids 110-126

**FIGURE 188**

TGTGTTTCCCTGCAGTCAGAATTTGGGACNGCAGGGGTTCCCGGACCTGATTTTGCAGCGGA  
ACGGGAAGGTTTTGTGGGACCCAGGTTGAAATGACGGTCATTTTTTTTCTTCTCCTTCNG  
GAGTCCTTNTGAGANGATGGTTTTGGGCGCAGCGGGAGCTAACCCGGTTTTTTGTNGCGATG  
GTAGCGGCGGTTTTTCGGCGGCCACCTTNTGCTGGGAGTGAGCGCCACCTTGAATCGGTTTTTC  
AATTCCAACGNTATCAAGAACCTGCCCCACCGNTGGGCGGCGCTGCGGGGCACCCAGGNTT  
TGCAGTCAGCGCCGCGCCGGGAATCCTGTACCCGGGCGGGAATAAGTACCAGACCATTGACA  
ATTACCAGCCGTACCCGTGCGCAGAGGACGAGGAGTGCGGCACTGATGAGTACTGCGCTAGT  
CCCACCCGCGGAGGGGANGCGGGCGTGCAAATNTGTNTNGCCTGCAGGAAGCGCCGAAAACG  
CTGCATGCGTCANGCTATGTGCTGCCCCGGAATTACTGCAAAAATGGAATATGTGTGTNTT  
CTGATCAAAATCATTTCCGAGGAGAAATTGAGGAAACCATCACTGAAAGCTTTGGTAATGAT  
CATAGCACCTTGGATGGG

**FIGURE 189A**

GAGGAACCTACCGGTACCGGCCGCGCTGGTAGTCGCCGGTGTGGCTGCACCTCACCAATC  
CCGTGCGCCGCGGGCTGGGCCGTCGGAGAGTGCCTGTGCTTCTCTCCTGCACGCGGTGCTTGG  
GCTCGGCCAGGCGGGTCCGCCGCGAGGTTTGGAGGATGGGGGAGTAGCTACAGGAAGCGAC  
CCCGCGATGGCAAGGTATATTTTGTGGAATGAAAAGGAAGTATTAGAAATGAGCTGAAGAC  
CATTCACAGATTAATATTTTGGGGACAGATTGTGATGCTTGATTACCCCTGAAGTAATG  
TAGACAGAAAGTTCTCAAATTTGCATATTACATCAACTGGAACCAGCAGTGAATCTTAATGTT  
CACTTAAATCAGAACTTGCATAAGAAAGAGAAATGGGAGTCTGGTTAAATAAAGATGACTATA  
TCAGAGACTTGAAAAGGATCATTCTCTGTTTTCTGATAGTGTATATGGCCATTTTAGTGGGC  
ACAGATCAGGATTTTACAGTTTACTTGGAGTGTCCAAAACCTGCAAGCAGTAGAGAAATAAG  
ACAAGCTTTCAGAAATTGGCATTGAAGTTACATCCTGATAAAAACCCGAATAACCCAAATG  
CACATGGCGATTTTTTAAATAAATAGAGCATATGAAGTACTCAAAGATGAAGATCTACGG  
AAAAAGTATGACAAATATGGAGAAAAGGACTTGAGGATAATCAAGGTGGCCAGTATGAAAG  
CTGGAACATTTATCGTTATGATTTTGGTATTTATGATGATGATCCTGAAATCATAACATTGG  
AAAGAAGAGAATTTGATGCTGCTGTTAATTCTGGAGAACTGTGGTTTGTAAATTTTACTCC  
CCAGGCTGTTCACTGCCATGATTTAGCTCCCACATGGAGAGACTTTGCTAAAGAAGTGGA  
TGGGTTACTTCGAATTGGAGCTGTTAACTGTGGTGATGATAGAATGCTTTGCCGAATGAAAG  
GAGTCAACAGCTATCCCAGTCTCTTCATTTTTCGGTCTGGAATGGCCCCAGTGAAATATCAT  
GGAGACAGATCAAAGGAGAGTTTAGTGAGTTTTGCAATGCAGCATGTTAGAAGTACAGTGAC  
AGAACTTTGGACAGGAAATTTGTCAACTCCATACAACTGCTTTTGCTGCTGGTATTGGCT  
GGCTGATCACTTTTTGTTCAAAAGGAGGAGATTGTTGACTTCACAGACACGACTCAGGCTT  
AGTGGCATGTTGTTCTCAACTCATTGGATGCTAAAGAAATATATTGGAAGTAATACATAA  
TCTTCCAGATTTTGAACACTTTTCGGCAAACACACTAGAGGATCGTTTGGCTCATCATCGGT  
GGCTGTTATTTTTTTCATTTTGGAAAAAATGAAAATCAAATGATCCTGAGCTGAAAAACTA  
AAAACCTCTACTTAAAAATGATCATATTCAAGTTGGCAGGTTTGAAGTTCCTCTGCACCAGA  
CATCTGTAGTAATCTGTATGTTTTTCAGCCGCTCTAGCAGTATTTAAAGGACAAGGAACCA  
AAGAATATGAAATTCATCATGGAAAGAAGATTCTATATGATATACTGCTTTGCCAAAGAA  
AGTGTGAATTCATGTTACCACGCTTGGACCTCAAATTTTCTGCTGCAATGACAAAGAACC  
ATGGCTTGTGATTTCTTTGCCCCCTGGTGTCCACCATGTCGAGCTTACTACCAGAGTTAC  
GAAGAGCATCAAATCTTCTTTATGGTCAGCTTAAGTTTGGTACACTAGATTGTACAGTTTCT  
GAGGGACTCTGTAACATGTATAACATTACGGCTTATCCAACAACAGTGGTATTCAACAGCTC  
CAACATTTCATGAGTATGAAGGACATCACTCTGCTGAACAAATCTTGGAGTTCATAGAGGATC  
TTATGAATCCTTCAGTGGTCTCCCTTACACCCACCACCTTCAACGAACTAGTTACACAAAGA  
AAACACAACGAAGTCTGGATGGTTGATTCTATTCTCCGTGGTGTATCCTTGCCAAGTCTT  
AATGCCAGAATGGAAAAGAATGGCCCGGACATTAAGTGGACTGATCAACGTGGGCAGTATAG  
ATTGCCAACAGTATCATTCTTTTTGTGCCCGAGGAAAACGTTCAAAGATACCCTGAGATAAGA  
TTTTTTCCCCCAAATCAAATAAAGCTTATCAGTATCACAGTTACAATGGTTGGAATAGGGA  
TGCTTATTCCTGAGAATCTGGGGTCTAGGATTTTTACCTCAAGTATCCACAGATCTAACAC  
CTCAGACTTTTCAGTGAAAAAGTTCTACAAGGGAAAAATCATTGGGTGATTGATTTCTATGCT  
CCTTGGTGTGGACCTTGCCAGAATTTTGCTCCAGAATTTGAGCTCTTGGCTAGGATGATTAA  
AGGAAAAGTGAAAGCTGGAAAAGTAGACTGTCAGGCTTATGCTCAGACATGCCAGAAAGCTG  
GGATCAGGGCCTATCCAACGTGTAAGTTTTATTTCTACGAAAGAGCAAAGAGAAATTTCAA  
GAAGAGCAGATAAATACCAGAGATGCAAAAGCAATCGCTGCCTTAATAAGTGAAAAATTGGA  
AACTCTCCGAAATCAAGGCAAGAGGAATAAGGATGAACCTTGAATAATGTTGAAGATGAAGAA  
AAAGTTTAAAGAAATTCTGACAGATGACATCAGAAGACACCTATTTAGAATGTTACATTTA  
TGATGGGAATGAATGAACATTATCTTAGACTTGCAGTTGTACTGCCAGAATTATCTACAGCA  
CTGGTGTAAGAAGGGTCTGCAAACTTTTTCTGTAAAGGGCCGTTTTATAAATATTTTAGA  
CTTTGCAAGGCTATAATATATGGTTCACACATGAGAACAAGAATAGAGTCATCATGTATTCTT  
TGTTATTTGCTTTTAAACAACCTTTAAAAAATATTTAAACGATTCTTAGCTCAGAGCCATACA  
AAAGTGAAGTGGATTTCAGTCCATGGACCATAGATTGCTGTCCCCCTCGACGGACTTATAATG  
TTTCAGGTGGCTGGCTTGAACATGAGTCTGCTGTGCTATCTACATAAATGCTTAAGTTGTAT  
AAAGTCCACTTTCCCTTTCACGTTTTTGGCTGACCTGAAAAGAGGTAAGTTAGTTTTTGGTC  
ACTTGTCTCTCTAAATAATGCTATCCCTAACCATATATTTATATTTGTTTTTAAACACCCA  
TGATGTGGCACAGTAACAAACCCGTGTTATGCTGTATTATTATGAGGAGATTCTTCATTGTT  
TTCTTTCTTCTCAAAGGTTGAAAAAATGCTTTTAATTTTTTACAGCCGAGAAACAGTGCAG

**FIGURE 189B**

CAGTATATGTGCACACAGTAAGTACACAAATTTGAGCAACAGTAAGTGCACAAATTCGTAG  
TTTGCTGTATCATCCAGGAAAACCTGAGGGAAAAAATTATAGCAATTAAGTGGGCATTGTA  
GAGTATCCTAAATATGTTATCAAGTATTTAGAGTTCCTATATTTTAAAGATATATGTGTTTCA  
GTATTTTCTGAAATTGCTTTTCATAGAAATTTTCCCACTGATAGTTGATTTTGGAGGCATCTA  
ATATTTACATATTTGCCTTCTGAACTTTGTTTTGACCTGTATCCTTTATTTACATTGGGTTT  
TTCTTTTCATAGTTTTGGTTTTTCACTCCTGTCCAGTCTATTTATTATTCAAATAGGAAAAAT  
TACTTTACAGGTTGTTTTACTGTAGCTTATAATGATACTGTAGTTATTCCAGTTACTAGTTT  
ACTGTCAGAGGGCTGCCTTTTTTCAGATAAATATTGACATAATAACTGAAGTTATTTTTATAA  
GAAAATCAAGTATATAAATCTAGGAAAGGGATCTTCTAGTTTCTGTGTTGTTTAGACTCAA  
GAATCACAAATTTGTCAGTAACATGTAGTTGTTTAGTTATAATTCAGAGTGTACAGAATGGT  
AAAAATCCAATCAGTCAAAGAGGTCAATGAATTAAAGGCTTGCAACTTTTTCAAAAAA  
AAAAA



**FIGURE 190**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56439

<subunit 1 of 1, 747 aa, 1 stop

<MW: 86127, pI: 7.46, NX(S/T): 2

MGVWLNKDDYIRDLKRIILCFLIVMAILVGTDQDFYSLLGVSKTASSREIRQAFKKLALKL  
HPDKNPNNPNAHGDFLKNRAYEVLKDEDLRKKYDKYGEKGLEDNQGQYESWNYRYDEFGI  
YDDDPETITLERREFDAAVNSGELWFVNFYSPGCSHCHDLAPTWRDFAKEVDGLLRIGAVNC  
GDDRMLCRMKGVNPSYSLFIFRSGMAPVKYHGDRSKESLVSFAMQHVRSTVTELWTGNFVNS  
IQTAFAAGIGWLITFCCKGGDCLTSQTRLRLSGMLFLNSLDAKEIYLEVIHNLPDFELLSAN  
TLEDRLAHRWLLFFHFGKNENSNDPELKKLKTLLKNDHIQVGRFDCSSAPDICSNLVVFQF  
SLAVFKGQGTKEYEIHGKKILYDILAFAKESVNSHVTTLGPQNFPANDKEPWLVDFFAPWC  
PPCRALLPELRRASNLLYGQLKFGTLDCTVHEGLCNMYNIQAYPTTVVFNQSNIEYEGHHS  
AEQILEFIEDLMNPSVVSLTPTTFNELVTQRKHNEVWMVDFYSPWCHPCQVLMPEWKRMART  
LTGLINVGSIDCQQYHSFCAQENVQRYPEIRFFPPKSNKAYQYHSYNGWNRDAYSRLRWGLG  
FLPQVSTDLTPQTFSEKVLQGNHWVIDFYAPWCGPCQNFAPFEFELLARMIKGKVKAGKVDC  
QAYAQTCQKAGIRAYPTVKFYFYERAKRNFQEEQINTRDAKAI AALISEKLETLRNQGKRKDEL

Important features:

Endoplasmic reticulum targeting sequence.

amino acids 744-747

Cytochrome c family heme-binding site signature.

amino acids 158-163

Nt-dnaJ domain signature.

amino acids 77-96

N-glycosylation site.

amino acids 484-487

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**FIGURE 191**

AGACAGTACCTCCTCCCTAGGACTACACAAGGACTGAACCAGAAGGAAGAGGACAGAGCAAA  
GCCATGAACATCATCCTAGAAATCCTTCTGCTTCTGATCACCATCATCTACTCCTACTTGGA  
GTCGTTGGTGAAGTTTTTTCATTCCTCAGAGGAGAAAATCTGTGGCTGGGGAGATTGTTCTCA  
TTACTGGAGCTGGGCATGGAATAGGCAGGCAGACTACTTATGAATTTGCAAAACGACAGAGC  
ATATTGGTTCTGTGGGATATTAATAAGCGCGGTGTGGAGGAACTGCAGCTGAGTGCCGAAA  
ACTAGGCGTCACTGCGCATGCGTATGTGGTAGACTGCAGCAACAGAGAAGAGATCTATCGCT  
CTCTAAATCAGGTGAAGAAAGAAGTGGGTGATGTAACAATCGTGGTGAATAATGCTGGGACA  
GTATATCCAGCCGATCTTCTCAGCACCAAGGATGAAGAGATTACCAAGACATTTGAGGTCAA  
CATCCTAGGACATTTTTTGGATCACAAAAGCACTTCTTCCATCGATGATGGAGAGAAATCATG  
GCCACATCGTCACAGTGGCTTCAGTGTGCGGCCACGAAGGGATTCCCTTACCTCATCCCATAT  
TGTTCCAGCAAATTTGCCGCTGTTGGCTTTTACAGAGGTCTGACATCAGAACTTCAGGCCTT  
GGGAAAAACTGGTATCAAAACCTCATGTCTCTGCCAGTTTTTGTGAATACTGGGTTACCA  
AAAATCCAAGCACAAGATTATGGCCTGTATTGGAGACAGATGAAGTCGTAAGAAGTCTGATA  
GATGGAATACTTACCAATAAGAAAATGATTTTTGTTCCATCGTATATCAATATCTTTCTGAG  
ACTACAGAAGTTTCTTCTGAACGCGCCTCAGCGATTTTAAATCGTATGCAGAAATATTCAAT  
TTGAAGCAGTGGTTGGCCACAAAATCAAAATGAAATGAATAAAATAAGCTCCAGCCAGAGATG  
TATGCATGATAATGATATGAATAGTTTGAATCAATGCTGCAAAGCTTTATTTTACATTTTTT  
TCAGTCCTGATAATATTAAAAACATTGGTTTGGCACTAGCAGCAGTCAAACGAACAAGATTA  
ATTACCTGTCTTCTGTTTCTCAAGAATATTTACGTAGTTTTTTCATAGGTCTGTTTTTCTT  
TCATGCTCTTAAAACTTCTGTGCTTACATAAACATACTTAAAGGTTTTCTTTAAGATAT  
TTTATTTTTTCCATTTAAAGGTGGACAAAAGCTACCTCCCTAAAAGTAAATACAAAGAGAACT  
TATTTACACAGGGAAGGTTAAGACTGTTCAAGTAGCATTCCAATCTGTAGCCATGCCACAG  
AATATCAACAAGAACACAGAATGAGTGCACAGCTAAGAGATCAAGTTTCAGCAGGCAGCTTT  
ATCTCAACCTGGACATATTTTAAGATTCAGCATTTGAAAGATTTCCCTAGCCTCTTCCTTTT  
TCATTAGCCCAAACGGTGCAACTCTATTCTGGACTTTATTACTTGATTCTGTCTTCTGTAT  
AACTCTGAAGTCCACCAAAGTGGACCCTCTATATTTCCCTCCCTTTTTATAGTCTTATAAGA  
TACATTATGAAAGGTGACCGACTCTATTTTAAATCTCAGAATTTTAAGTTCTAGCCCCATGA  
TAACCTTTTTTCTTTGTAATTTATGCTTTCATATATCCTTGGTCCCAGAGATGTTTAGACAAT  
TTTAGGCTCAAAAATTAAAGCTAACACAGGAAAAGGAAGTGTACTGGCTATTACATAAGAAA  
CAATGGACCCAAGAGAAGAA

**FIGURE 192**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56409

<subunit 1 of 1, 300 aa, 1 stop

<MW: 33655, pI: 9.31, NX(S/T): 1

MNIILEILLLLITIIYSYLESVLKFFIPQRRKSVAGEIVLITGAGHGIGRQTTYEFAKRQSI  
LVLWDINKRGVEETAAECKRLGVTAHAYVVDCSNREEIYRSLNQVKKEVGDTVIVVNNAGTV  
YPADLLSTKDEEITKTFEVNILGHFWITKALLPSMMERNHGHIVTVASVCGHEGIPYLIPYC  
SSKFAAVGFHRGLTSELQALGKTGIKTSCLCPVFVNTGFTKNPSTRLWPVLETDEVVRSID  
GILTNNKMIFVPSYINIFLRLQKFLPERASAILNRMQNIQFEAVVGHKIKMK

**Important features:**

**Signal peptide:**

amino acids 1-19

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 30-33 and 58-61

**Short-chain alcohol dehydrogenase family protein**

amino acids 165-202, 37-49, 112-122 and 210-219

**FIGURE 193**

CGGCGGCGGCTGCGGGCGCGAGGTGAGGGGCGCGAGGTGAGGGGCGCGAGGTTCCCAGCAGG  
ATGCCCCGGCTCTGCAGGAAGCTGAAGTGAGAGGCCCGGAGAGGGGCCAGCCCGCCGGGGC  
AGGATGACCAAGGCCCCGGCTGTTCCGGCTGTGGCTGGTGCTGGGGTCGGTGTTTCATGATCCT  
GCTGATCATCGTGTACTGGGACAGCGCAGGCGCCGCGCACTTCTACTTGACACAGTCCTTCT  
CTAGGCCGCACACGGGGCCGCCGCTGCCACGCCGGGCGGACAGGGACAGGGAGCTCACG  
GCCGACTCCGATGTGACGAGTTTCTGGACAAGTTTCTCAGTGCTGGCGTGAAGCAGAGCGA  
CCTTCCCAGAAAGGAGACGGAGCAGCCGCCTGCGCCGGGAGCATGGAGGAGAGCGTGAGAG  
GCTACGACTGGTCCCCGCGCGACGCCCGGCGCAGCCCAGACCAGGGCCGGCAGCAGGCGGAG  
CGGAGGAGCGTGCTGCGGGGCTTCTGCGCCAACCTCCAGCCTGGCCTTCCCCACCAAGGAGCG  
CGCATTCGACGACATCCCCAACTCGGAGCTGAGCCACCTGATCGTGGACGACCGGCACGGGG  
CCATCTACTGCTACGTGCCCCAAGGTGGCCTGCACCAACTGGAAGCGCGTGATGATCGTGCTG  
AGCGGAAGCCTGCTGCACCGCGGTGCGCCCTACCGCGACCCGCTGCGCATCCCGCGCGAGCA  
CGTGACAACGCCAGCGCGCACCTGACCTTCAACAAGTTCTGGCGCCGCTACGGGAAGCTCT  
CCCGCCACCTCATGAAGGTCAAGCTCAAGAAGTACACCAAGTTCTTCTGCGCGACCCC  
TTCGTGCGCCTGATCTCCGCCTTCCGCAGCAAGTTCGAGCTGGAGAACGAGGAGTTCTACCG  
CAAGTTCGCCGTGCCCCATGCTGCGGCTGTACGCCAACCACACCAGCCTGCCCGCCTCGGCGC  
GCGAGGCCTTCCGCGCTGGCCTCAAGGTGTCCTTCGCCAACTTCATCCAGTACCTGCTGGAC  
CCGCACACGGAGAAGCTGGCGCCCTTCAACGAGCACTGGCGGCAGGTGTACCGCCTCTGCCA  
CCCGTGCCAGATCGACTACGACTTCGTGGGGAAGCTGGAGACTCTGGACGAGGACGCCGCGC  
AGCTGCTGCAAGCTACTCCAGGTGGACCGGCAGCTCCGCTTCCCCCGAGCTACCGGAACAGG  
ACCGCCAGCAGCTGGGAGGAGGACTGGTTCGCCAAGATCCCCCTGGCCTGGAGGCAGCAGCT  
GTATAAACTCTACGAGGCCGACTTTGTTCTCTTCGGCTACCCCAAGCCCGAAAACCTCCTCC  
GAGACTGAAAGCTTTCGCGTTGCTTTTTCTCGCGTGCTTGGAACTGACGCACGCGCACTCC  
AGTTTTTTTATGACCTACGATTTTGCAATCTGGGCTTCTTGTTCACTCCACTGCCTCTATCC  
ATTGAGTACTGTATCGATATTGTTTTTAAAGATTAATATATTTTCAGGTATTTAATACGA

**FIGURE 194**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56112

<subunit 1 of 1, 414 aa, 1 stop

<MW: 48414, pI: 9.54, NX(S/T): 4

MTKARLFRLWLVLGSMILLIIVYWDSAGAAHFYLHTSFSRPHTGPPPLPTPGPDRDRELT  
DSDVDEFLDKFLSAGVKQSDLPRKETEQQPPAGSMEE SVRGYDWSPRDARRSPDQGRQQAER  
RSVLRGFCANSSLAFTKERAFFDDIPNSEL SHLIVDDRHGAIYCYVPKVACTNWKRVMI VLS  
GSL LHRGAPYRDPLRIPREHVHNASAHLT FNKFWRRYGKLSRHLMKVKLKKYTKFLEVRDPF  
VRLISAFRSKFELENEEFYRKFAVPMRLRYANHTSLPASAREAFRAGLKVSFANFIQYLLDP  
HTEKLAPFNEHWRQVYRLCHPCQIDYDFVGKLETLD EDAQQLQLLQVDRQLRFPPSYRNRT  
ASSWEEDWFAKIPLAWRQQLYKLYEADFVLF GYPKPENLLRD

**Important features:**

**Signal peptide:**

amino acids 1-31

**N-glycosylation sites.**

amino acids 134-137, 209-212, 280-283 and 370-373

**TNFR/NGFR family cysteine-rich region protein**

amino acids 329-332

**FIGURE 195**

TCGGGCCAGAATTCGGCACGAGGCGGCACGAGGGCGACGGCCTCACGGGGCTTTGGAGGTGA  
AAGAGGGCCAGAGTAGAGAGAGAGAGACCGACGTACACGGGATGGCTACGGGAACGCGCT  
ATGCCGGGAAGGTGGTGGTCGTGACCGGGGGCGGGCGGGCATCGGAGCTGGGATCGTGCGC  
GCCTTCGTGAACAGCGGGGCCCCGAGTGGTTATCTGCGACAAGGATGAGTCTGGGGGCGGGC  
CCTGGAGCAGGAGCTCCCTGGAGCTGTCTTTATCCTCTGTGATGTGACTCAGGAAGATGATG  
TGAAGACCCTGGTTTCTGAGACCATCCGCCGATTGGCCGCCTGGATTGTGTTGTCAACAAC  
GCTGGCCACCACCCACCCCCACAGAGGCCTGAGGAGACCTCTGCCCAGGGATTCCGCCAGCT  
GCTGGAGCTGAACCTACTGGGGACGTACACCTTGACCAAGCTCGCCCTCCCCTACCTGCGGA  
AGAGTCAAGGGAATGTCATCAACATCTCCAGCCTGGTGGGGGCAATCGGCCAGGCCCAGGCA  
GTTCCCTATGTGGCCACCAAGGGGGCAGTAACAGCCATGACCAAAGCTTTGGCCCTGGATGA  
AAGTCCATATGGTGTCCGAGTCAACTGTATCTCCCCAGGAAACATCTGGACCCCGCTGTGGG  
AGGAGCTGGCAGCCTTAATGCCAGACCCTAGGGCCACAATCCGAGAGGGCATGCTGGCCCAG  
CCTACTGGGCGCATGGGCCAGCCCGCTGAGGTCGGGGCTGCGGCAGTGTTCTGGCCTCCGA  
AGCCAACCTTCTGCACGGGCATTGAACTGCTCGTGACGGGGGGTGCAGAGCTGGGGTACGGGT  
GCAAGGCCAGTCGGAGCACCCCCGTGGACGCCCCGATATCCCTTCCTGATTTCTCTCATTT  
CTACTTGGGGCCCCCTTCCCTAGGACTCTCCCACCCAACTCCAACCTGTATCAGATGCAGC  
CCCCAAGCCCTTAGACTCTAAGCCCAGTTAGCAAGGTGCCGGGTACCCTGCAGGTTCCCAT  
AAAAACGATTTCAGCC

**FIGURE 196**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56045

<subunit 1 of 1, 270 aa, 1 stop

<MW: 28317, pI: 6.00, NX(S/T): 1

MATGTRYAGKVVVVTGGGRGIGAGIVRAFVNSGARVVICDKDESGGRALEQELPGAVFILCD  
VTQEDDVKTLVSETIRRFGRLLDCVVNNAGHHPPQRPETSAQGFRQLLELNLLGTYTLTKL  
ALPYLRKSQGNVINISSLVGAIGQAQAVPYVATKGAVTAMTKALALDESPYGVRVNCISPGN  
IWTPLWEELAALMPDPRATIREGMLAQPLGRMGQPAEVGAAVFLASEANFCTGIELLVTTGG  
AELGYGCKASRSTPVDAPDIPS

**Important features:**

**N-glycosylation site.**

amino acids 138-141

**Short-chain alcohol dehydrogenase family protein**

amino acids 10-22, 81-91, 134-171 and 176-185

**FIGURE 197**

AGGCGGGCAGCAGCTGCAGGCTGACCTTGCAGCTTGGCGGAATGGACTGGCCTCACAACTG  
CTGTTTCTTCTTACCATTTCCATCTTCCTGGGGCTGGGCCAGCCCAGGAGCCCCAAAAGCAA  
GAGGAAGGGGCAAGGGCGGCCTGGGCCCCCTGGCCCCCTGGCCCTCACCAGGTGCCACTGGACC  
TGGTGTACGGATGAAACCGTATGCCCCGATGGAGGAGTATGAGAGGAACATCGAGGAGATG  
GTGGCCCAGCTGAGGAACAGCTCAGAGCTGGCCCAGAGAAAGTGTGAGGTCAACTTGCAGCT  
GTGGATGTCCAACAAGAGGAGCCTGTCTCCCTGGGGCTACAGCATCAACCACGACCCCAGCC  
GTATCCCCGTGGACCTGCCGGAGGCACGGTGCCTGTGTCTGGGCTGTGTGAACCCCTTCACC  
ATGCAGGAGGACCGCAGCATGGTGAGCGTGCCGGTGTTCAGCCAGGTTCTGTGCGCCGCCG  
CCTCTGCCCCGCCACCGCCCCGCACAGGGCCTTGCCGCCAGCGCGCAGTCATGGAGACCATCG  
CTGTGGGCTGCACCTGCATCTTCTGAATCACCTGGCCCAGAAGCCAGGCCAGCAGCCCGAGA  
CCATCCTCCTTGCACCTTTGTGCCAAGAAAGGCCTATGAAAAGTAAACACTGACTTTTGAAA  
GCAAG



**FIGURE 198**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA59294

<subunit 1 of 1, 180 aa, 1 stop

<MW: 20437, pI: 9.58, NX(S/T): 1

MDWPHNLLFLLTISIFLGLGQPRSPKSKRKGQGRPGPLAPGPHQVPLDLVSRMKPYARMEEY  
ERNIEEMVAQLRNSSELAQRKCEVNLQLWMSNKRSLSPWGYSINHDPRI PVDLPEARCLCL  
GCVNPFTMQEDRSMVSVPVFSQVPVRRRLCPPPPRTGPCRQRAVMETIAVGCTCIF

**Important features:**

**Signal peptide:**

amino acids 1-20

**N-glycosylation site.**

amino acids 75-78

**Homologous region to IL-17**

amino acids 96-180.

**FIGURE 199**

GC GCCGCCAGGCGTAGGCGGGGTGGCCCTTGCGTCTCCCGCTTCCTTGAAAAACCCGGCGGG  
CGAGCGAGGCTGCGGGCCGGCCGCTGCCCTTCCCCACACTCCCCGCCGAGAAGCCTCGCTCG  
GCGCCCAACATGGCGGGGTGGGCGCTGCGGCCCGCAGCTAACGGCGCTCCTGGCCGCCTGGAT  
CGCGGCTGTGGCGGCGACGGCAGGCCCCGAGGAGGCCGCGCTGCCGCCGGAGCAGAGCCGGG  
TCCAGCCCATGACCGCCTCCAAC TGGACGCTGGTGATGGAGGGCGAGTGGATGCTGAAATTT  
TACGCCCCATGGTGTCCATCCTGCCAGCAGACTGATTCAGAATGGGAGGCTTTTGCAAAGAA  
TGGTGAAATACTTCAGATCAGTGTGGGGAAGGTAGATGTCATTCAAGAACCAGGTTTGAGTG  
GCCGCTTCTTTGTCACCACTCTCCCAGCATT TTTTCATGCAAAGGATGGGATATTCCGCCGT  
TATCGTGGCCCAGGAATCTTCGAAGACCTGCAGAATTATATCTTAGAGAAGAAATGGCAATC  
AGTCGAGCCTCTGACTGGCTGGAAATCCCCAGCTTCTCTAACGATGTCTGGAATGGCTGGTC  
TTTTTAGCATCTCTGGCAAGATATGGCATCTTCACAAC TATTTACAGTGACTCTTGGAATT  
CCTGCTTGGTGTTCTTATGTGTTTTTCGTCATAGCCACCTTGGTTTTTGGCCTTTTTATGGG  
TCTGGTCTTGGTGGTAATATCAGAATGTTTCTATGTGCCACTTCCAAGGCATTTATCTGAGC  
GTTCTGAGCAGAATCGGAGATCAGAGGAGGCTCATAGAGCTGAACAGTTGCAGGATGCGGAG  
GAGGAAAAAGATGATTCAAAATGAAGAAGAAAACAAAGACAGCCTTG TAGATGATGAAGAAGA  
GAAAGAAGATCTTGGCGATGAGGATGAAGCAGAGGAAGAAGAGGAGGAGGACAACCTTGGCTG  
CTGGTGTGGATGAGGAGAGAAGTGAGGCCAATGATCAGGGGGCCCCAGGAGAGGACGGTGTG  
ACCCGGGAGGAAGTAGAGCCTGAGGAGGCTGAAGAAGGCATCTCTGAGCAACCTGCCCAGC  
TGACACAGAGGTGGTGGAAAGACTCCTTGAGGCAGCGTAAAAGTCAGCATGCTGACAAGGGAC  
TG TAGATTTAATGATGCGTTTTCAAGAATACACACCAAAACAATATGTCAGCTTCCCTTTGG  
CCTGCAGTTTGTACCAAATCCTTAATTTTTCTGAATGAGCAAGCTTCTCTTAAAGATGCT  
CTCTAGTCATTTGGTCTCATGGCAGTAAGCCTCATGTATACTAAGGAGAGTCTTCCAGGTGT  
GACAATCAGGATATAGAAAAACAAACGTAGTGTGGGATCTGTTTGGAGACTGGGATGGGAA  
CAAGTTCATTTACTTAGGGGTCAGAGAGTCTCGACCAGAGGAGGCCATTCCCAGTCCTAATC  
AGCACCTTCCAGAGACAAGGCTGCAGGCCCTGTGAAATGAAAGCCAAGCAGGAGCCTTGGCT  
CCTGAGCATCCCCAAAGTGTAACGTAGAAGCCTTGCATCCTTTTCTTGTTGTAAAGTATTTAT  
TTTTGTCAAATTGCAGGAAACATCAGGCACCACAGTGCATGAAAAATCTTTCACAGCTAGAA  
ATTGAAAGGGCCTTGGGTATAGAGAGCAGCTCAGAAGTCATCCCAGCCCTCTG AATCTCCTG  
TGCTATGTTTTATTTCTTACCTTTAATTTTTCCAGCATTTCCACCATGGGCATT CAGGCTCT  
CCACACTCTTCACTATTATCTCTTGGTCAGAGGACTCCAATAACAGCCAGGTTTACATGAAC  
TGTGTTTGTTCATTCTGACCTAAGGGGTTTAGATAATCAGTAACCATAACCCCTGAAGCTGT  
GACTGCCAAACATCTCAAATGAAATGTTGTGGCCATCAGAGACTCAAAAGGAAGTAAGGATT  
TTACAAGACAGATTAAAAAAAATTGTTTTGTCCAAAATATAGTTGTTGTTGATTTTTTTTT  
AAGTTTTCTAAGCAATATTTTTCAAGCCAGAAGTCCTCTAAGTCTTGCCAGTACAAGGTAGT  
CTTGTTGAAGAAAAGTTGAATACTGTTTTGTTTTTCATCTCAAGGGGTTCCCTGGGTCTTGAAC  
TACTTTAATAATAACTAAAAAACCACTCTGATTTTCTTCAGTGATGTGCTTTTGGTGAAA  
GAATTAATGAACCTCAGTACCTGAAAGTGAAAGATTTGATTTTGTTCATCTTCTGTAAATC  
TTCCAAAGAATTATATCTTTGTAAATCTCTCAATACTCAATCTACTGTAAGTACCCAGGGAG  
GCTAATTTCTTT

**FIGURE 200**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA56433

<subunit 1 of 1, 349 aa, 1 stop

<MW: 38952, pI: 4.34, NX(S/T): 1

MAGGRCGPQLTALLAAWIAAVAATAGPEEAALPPEQSRVQPMTASNWTLVMEGEWMLKIFYAP  
WCPSCQQT DSEWEAFAKNGEILQISVGKVDVIQEPGLSGRFFVTTLPAFFHAKDGI FRRYRG  
PGIFEDLQNYILEKKWQSVEPLTGWKSPASLTMSGMAGLFSISGKIWHLHNYFTVTLGIPAW  
CSYVFFVIATLVFGLFMGLVLVVISSECFYVPLPRHLSESEQNRRSEEAHRAEQLQDAEEEEK  
DDSNEEENKDSLVDDEEEKEDLGDEDEAEEDNLAAGVDEERSEANDQGPPGEDGVTRE  
EVEPEEAEEGISEQPCPADTEVVEDSLRQRKSKHADKGL

**Important features:**

**Signal peptide:**

amino acids 1-22

**Transmembrane domain:**

amino acids 191-211

**N-glycosylation site.**

amino acids 46-49

**Thioredoxin family proteins.** (homologous region to disulfide isomerase)

amino acids 56-72

**Flavodoxin proteins**

amino acids 173-187

**FIGURE 201**

ATCTGGTTGAACTACTTAAGCTTAATTTGTTAACTCCGGTAAGTACCTAGCCCACATGATT  
TGA CTCAGAGATTCTCTTTTGTCCACAGACAGTCATCTCAGGGGCAGAAAGAAAAGAGCTCC  
CAAATGCTATATCTATT CAGGGGCTCTCAAGAACAATGGAATATCATCCTGATTTAGAAAAT  
TTGGATGAAGATGGATATACTCAATTACACTTCGACTCTCAAAGCAATACCAGGATAGCTGT  
TGTTTCAGAGAAAGGATCGTGTGCTGCATCTCCTCCTTGGCGCCTCATTGCTGTAATTTTGG  
GAATCCTATGCTTGTTAATACTGGTGATAGCTGTGGTCCTGGGTACCATGGGGGTTCTTTCC  
AGCCCTTGTCTCCTAATTGGATTATATATGAGAAGAGCTGTTATCTATT CAGCATGTCACT  
AAATTCCTGGGATGGAAGTAAAAGACAATGCTGGCAACTGGGCTCTAATCTCTAAAGATAG  
ACAGCTCAAATGAATTGGGATTTATAGTAAAACAAGTGTCTTCCCAACCTGATAATTCATTT  
TGGATAGGCCTTTCTCGGCCCCAGACTGAGGTACCATGGCTCTGGGAGGATGGATCAACATT  
CTCTTCTAACTTATTT CAGATCAGAACCACAGCTACCCAAGAAAACCCATCTCCAAATTGTG  
TATGGATTACAGTGT CAGTCATTTATGACCAACTGTGTAGTGTGCCCTCATATAGTATTTGT  
GAGAAGAAGTTTTCAATGTAAGAGGAAGGGTGGAGAAGGAGAGAGAAATATGTGAGGTAGTA  
AGGAGGACAGAAAACAGAACAGAAAAGAGTAACAGCTGAGGTCAAGATAAATGCAGAAAATG  
TTTAGAGAGCTTGGCCAACTGTAATCTTAACCAAGAAATTGAAGGGAGAGGCTGTGATTTCT  
GTATTTGTGCGACCTACAGGTAGGCTAGTATTATTTTTCTAGTTAGTAGATCCCTAGACATGG  
AATCAGGGCAGCCAAGCTTGAGTTTTTATTTTTTATTTATTTTATTTTGGAGATAGGGTCT  
CACTTTGTTACCCAGGCTGGAGTGCAGTGGCACAATCTCGACTCACTGCAGCTATCTCTCGC  
CTCAGCCCCCTCAAGTAGCTGGGACTACAGGTGCATGCCACCATGCCAGGCTAATTTTTGGTG  
TTTTTTGTAGAGACTGGGTTTTGCCATGTTGACCAAGCTGGTCTCTAACTCCTGGGCTTAAG  
TGATCTGCCCGCCTTGGCCTCCCAAAGTGCTGGGATTACAGATGTGAGCCACCACACCTGGC  
CCCAAGCTTGAATTTTCATTCTGCCATTGACTTGGCATTACCTTGGGTAAGCCATAAGCGA  
ATCTTAATTTCTGGCTCTATCAGAGTTGTTTCATGCTCAACAATGCCATTGAAGTGCACGGT  
GTGTTGCCACGATTTGACCCTCAACTCTAGCAGTATATCAGTTATGAAGTGAAGGTTGAAT  
ATATTTCTGAATAGCTAAATGAAGAAATGGGAAAAATCTTCACCACAGTCAGAGCAATTTT  
ATTATTTTCATCAGTATGATCATAATTATGATTATCATCTTAGTAAAAAGCAGGAATCCTA  
CTTTTTCTTTATCAATTAAATAGCTCAGAGAGTACATCTGCCATATCTCTAATAGAATCTTT  
TTTTTTTTTTTTTTTTTTTTTGAGACAGAGTTTCGCTCTTGTGCCCAGGCTGGAGTSCAACGG  
CACGATCTCGGCTCACCGCAACCTCCGCCCCCTGGGTTCAAGCAATTCTCTGCTCAGCCT  
CCCAAGTAGCTGGGATTACAGTCAGGCACCACCACACCCGGCTAATTTTGTATTTTGTAGT  
AGAGACAGGGTTTCTCCATGTGCGGT CAGGGTAGTCCCGAACTCCTGACCTCAAGTGATCTGC  
CTGCCCTCGGCTCCCAAGTGCTGGGATTACAGGCGTGAGCCACTGCACCCAGCCTAGAATCT  
TGTATAATATGTAATTGTAGGGAACTGCTCTCATAGGAAAGTTTTCTGCTTTTTTAAATACA  
AAAATACATAAAAAATACATAAAATCTGATGATGAATATAAAAAAGTAACCAACCTCATTGGA  
ACAAGTATTAACATTTTGGAAATATGTTTTATTAGTTTTGTGATGTACTGTTTTACAATTTTT  
ACCATTTTTTTT CAGTAATTACTGTAAAATGGTATTATTGGAATGAACTATATTTCTCATG  
TGCTGATTTGTCTTATTTTTTTT CATACTTCCCACTGGTGCTATTTTTATTTCCAATGGATA  
TTTCTGTATTACTAGGGAGGCATTTACAGTCCTCTAATGTTGATTAATATGTGAAAAGAAAT  
TGTACCAATTTTACTAAATTATGCAGTTTAAATGGATGATTTTATGTTATGTGGATTTTCAT  
TTCAATAAAAAAAACTCTTATCAAAAAAAATTTTTTTTTTTTTTTTTTTTTTTTTTTTTTT

**FIGURE 202**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA53912

<subunit 1 of 1, 201 aa, 1 stop

<MW: 22563, pI: 4.87, NX(S/T): 1

MEYHPDLENLDEDGYTQLHFDSQSNTRIAVVSEKGS CAASPPWRLIAVILGILCLVILVIAV  
VLGTMGVLS SPCPPNWIIYEKSCYLFMSLNSWDGSKRQCWQLGSNLLKIDSSNELGFIVKQ  
VSSQPDNSFWIGLSRPQTEVPWLWEDGSTFSSNLFQIRTTATQENPSPNCVWIHVSVIYDQL  
CSVPSYSICEKKFSM

**Important features:**

**Type II transmembrane domain:**

amino acids 45-65

**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 197-200

**N-myristoylation sites.**

amino acids 35-40 and 151-156

**Homologous region to LDL receptor**

amino acids 34-67 and 70-200.

## FIGURE 203A

GGAAGGGGAGGAGCAGGCCACACAGGCCACAGGCCGGTGAGGGACCTGCCCAGACCTGGAGGG  
TCTCGCTCTGTACACAGGCTGGAGTGCAGTGGTGTGATCTTGGCTCATCGTAACCTCCACC  
TCCCGGGTTCAAGTGATTCTCATGCCTCAGCCTCCCGAGTAGCTGGGATTACAGGTGGTGAC  
TTCCAAGAGTGACTCCGTCCGAGGAAAATGACTCCCCAGTCGCTGCTGCAGACGACACTGTT  
CCTGCTGAGTCTGCTCTTCTTCTGGTCCAAGGTGCCACGGCAGGGGCCACAGGGAAGACTTTC  
GCTTCTGCAGCCAGCGGAACCAGACACACAGGAGCAGCCTCCACTACAAACCCACACCAGAC  
CTGCGCATCTCCATCGAGAACTCCGAAGAGGCCCTCACAGTCCATGCCCTTTCCCTGCAGC  
CCACCCTGCTTCCCGATCCTTCCCTGACCCAGGGGCCCTTACCACTTCTGCCTCTACTGGA  
ACCGACATGCTGGGAGATTACATCTTCTCTATGGCAAGCGTGACTTCTTGCTGAGTGACAAA  
GCCTCTAGCCTCCTCTGCTTCCAGCACAGGAGGAGAGCCTGGCTCAGGGCCCCCGCTGTT  
AGCCACTTCTGTCACTCCTGGTGGAGCCCTCAGAACATCAGCCTGCCAGTGCCGCCAGCT  
TCACCTTCTCCTTCCACAGTCTTCCCCACACGGCCGCTCACAATGCCTCGGTGGACATGTGC  
GAGCTCAAAAGGGACCTCCAGCTGCTCAGCCAGTTCTGAAGCATCCCCAGAAGGCCCTAAG  
GAGGCCCTCGGCTGCCCCGCCAGCCAGCAGTTGCAGAGCCTGGAGTCGAAACTGACCTCTG  
TGAGATTCTATGGGGGACATGGTGTCTTTCGAGGAGGACCGGATCAACGCCACGGTGTGGAAG  
CTCCAGCCCACAGCCGGCCTCCAGGACCTGCACATCCACTCCCGGCAGGAGGAGGAGCAGAG  
CGAGATCATGGAGTACTCGGTGCTGCTGCCTCGAACACTCTTCCAGAGGACGAAAGGCCGGA  
GCGGGGAGGCTGAGAAGAGACTCCTCCTGGTGGACTTCAGCAGCCAAGCCCTGTTCCAGGAC  
AAGAATTCCAGCCAAGTCTTGGGTGAGAAGGTCTTGGGGATTGTGGTACAGAACACCAAAGT  
AGCCAACCTCACGGAGCCCGTGGTGTCTACTTCCAGCACAGCTACAGCCGAAGAATGTGA  
CTCTGCAATGTGTGTCTTGGGTTGAAGACCCACATTGAGCAGCCCGGGGCATTGGAGCAGT  
GCTGGGTGTGAGACCGTCAGGAGAGAAACCCAAACATCCTGCTTCTGCAACCACTTGACCTA  
CTTTGCAGTGCTGATGGTCTCCTCGGTGGAGGTGGACGCCGTGCACAAGCACTACCTGAGCC  
TCCTCTCCTACGTGGGCTGTGTCTCTGCTTCCCTGGCCTGCCTTGTCAACCACTTGACCTA  
CTCTGCTCCAGGGTGGCCCTGCCGTGCAGGAGGAAACCTCGGGACTACACCATCAAGGTGCA  
CATGAACCTGCTGCTGGCCGTCTTCTGCTGGACACGAGCTTCTGCTCAGCGAGCCGGTGG  
CCCTGACAGGCTCTGAGGCTGGCTGCCGAGCCAGTGCCATCTTCTGCACTTCTCCCTGCTC  
ACCTGCCTTTCTGGATGGGCCTCGAGGGGTACAACCTCTACCGACTCGTGGTGGAGGTCTT  
TGGCACCTATGTCCCTGGCTACCTACTCAAGCTGAGCGCCATGGGCTGGGGCTTCCCATCT  
TTCTGGTGACGCTGGTGGCCCTGGTGGATGTGGACAACATATGGCCCATCATCTTGGCTGTG  
CATAGGACTCCAGAGGGCGTCATCTACCCTTCCATGTGCTGGATCCGGGACTCCCTGGTCTAG  
CTACATCACCAACCTGGGCCTCTTCCAGCCTGGTGTCTTCTGTTCAACATGGCCATGCTAGCCA  
CCATGGTGGTGCAGATCTGCGGCTGCGCCCCACACCCAAAAGTGGTACATGTGCTGACA  
CTGCTGGGCCTCAGCCTGGTCTTGGCCTGCCCTGGGCCTTGATCTTCTTCTCCTTTGCTTC  
TGGCACCTTCCAGCTTGTGCTCTCTACCTTTTTCAGCATCATCACCTCCTTCCAAGGCTTCC  
TCATCTTCTATCTGGTACTGGTCCATGCGGCTGCAGGCCCGGGGTGGCCCTCCCCTCTGAAG  
AGCAACTCAGACAGCGCCAGGCTCCCCATCAGCTCGGGCAGCACCTCGTCCAGCCGCATCTA  
GGCCTCCAGCCCACCTGCCCATGTGATGAAGCAGAGATGCGGCCTCGTCGCACACTGCCTGT  
GGCCCCCGAGCCAGGCCAGGCCAGGCCAGTCAGCCGCAGACTTTGGAAAGCCCAACGACC  
ATGGAGAGATGGGCCGTTGCCATGGTGGACGGAATCCCGGGCTGGGCTTTTGAATTGGCCTT  
GGGGACTACTCGGCTCTCACTCAGCTCCACGGGACTCAGAAGTGCGCCGCCATGCTGCCTA  
GGGTACTGTCCCCACATCTGTCCCAACCCAGCTGGAGGCCTGGTCTCTCCTTACAACCCCTG  
GGCCAGCCCTCATTGCTGGGGGCCAGGCCTTGGATCTTGAGGGTCTGGCACATCCTTAATC  
CTGTGCCCCCTGCCTGGGACAGAAATGTGGCTCCAGTTGCTCTGTCTCTCGTGGTCAACCTGA  
GGGCACTCTGCATCCTCTGTCAATTTAACCCTCAGGTGGCACCCAGGGCGAATGGGGCCAGG  
GCAGACCTTCAGGGCCAGAGCCCTGGCGGAGGAGAGGCCCTTTGCCAGGAGCACAGCAGCAG  
CTCGCCTACCTCTGAGCCAGGCCCTCCCTCCCTCAGCCCCCAGTCTCCCTCCATCTT  
CCCTGGGGTTCTCCTCCTCTCCCAGGGCCTCCTTGCTCCTTCGTTACAGCTGGGGGTCCCC  
GATTCCAATGCTGTTTTTTGGGGAGTGGTTTTCCAGGAGCTGCCTGGTGTCTGCTGTAAATGT  
TTGTCTACTGCACAAGCCTCGGCCTGCCCTGAGCCAGGCTCGGTACCGATGCGTGGGCTGG  
GCTAGGTCCCTCTGTCCATCTGGGCCTTTGTATGAGCTGCATTGCCCTTGCTCACCTGACC  
AAGCACACGCCTCAGAGGGGCCCTCAGCCTCTCCTGAAGCCCTCTTGTGGCAAGAACTGTGG  
ACCATGCCAGTCCCGTCTGGTTTTCCATCCCACTCCAAGGACTGAGACTGACCTCCTCTG  
GTGACACTGGCCTAGAGCCTGACACTCTCCTAAGAGGTTCTCTCCAAGCCCCCAAATAGCTC

**FIGURE 203B**

CAGGCGCCCTCGGCCGCCCATCATGGTTAATTCTGTCCAACAAACACACACGGGTAGATTGC  
TGGCCTGTTGTAGGTGGTAGGGACACAGATGACCGACCTGGTCACTCCTCCTGCCAACATTC  
AGTCTGGTATGTGAGGCGTGCCTGAAGCAAGAACTCCTGGAGCTACAGGGACAGGGAGCCAT  
CATTCCTGCCTGGGAATCCTGGAAGACTTCCTGCAGGAGTCAGCGTTCAATCTTGACCTTGA  
AGATGGGAAGGATGTTCTTTTTACGTACCAATTCTTTTGTCTTTTGATATTAAAAAGAAGTA  
CATGTTTCATTGTAGAGAATTTGGAACTGTAGAAGAGAATCAAGAAGAAAAATAAAAATCAG  
CTGTTGTAATCGCCTAGCAA  
AAA

**FIGURE 204**

</usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA50921  
<subunit 1 of 1, 693 aa, 1 stop  
<MW: 77738, pI: 8.87, NX(S/T): 7  
MTPQSLQLQTTLFLLSLLFLVQGAHGRGHREDFRFC SQRNQTHRSSLHYKPTPDLRISIENSE  
EALT VHAPFPAAHPASRSFPDPRGLYHFCLYWNRHAGRLHLLYGKRD FLLSDKASSLLCFQH  
QEESLAQGPPLLATSVTSWWSPQNI SLPSAASFTFSFHSPHTAAHNASVDMCELKRDLQLL  
SQFLKHPQKASRRPSAAPASQQLOQSLESKLT SVRFMGDMVSFEEDRINATVWKLQPTAGLQD  
LHIHSRQEEEQSEIMEYSVLLPRTL FQRTKGRSGEAEKRLLLVD FSSQALFQDKNSSQVLGE  
KVLGIVVQNTKVANLTEPVVLT FQHQLQPKNVT LQCVFWVEDPTLSSPGHWSSAGCETVRRE  
TQTSCFCNHLTYFAVLMVSSVEVDAVHKHYLSLLSYVGC VVSALACLVTIAAYLCSRVP LPC  
RRKPRDYTIKVHMNLLLAVFLLDTSFLLSEPVALTGSEAGCRASAI FLHFSLLTCLSWMGLE  
GYNLYRLVVEVFGTYVPGYLLKLSAMGWGFPIFLVTLVALVDVDNYGPI ILAVHRTPEGVIY  
PSMCWIRDSLVSYITNLGLFSLVFLFN MAMLATMVVQILRLRPHTQKWSHVL TLLGLSLVLG  
LPWALIFFSFASGTFQLVVLYLFSIITSFOGFLIFIWYWSMRLQARGGPSPLKSN SDSARLP  
ISSGSTSSSRI

**Important features:****Signal peptide:**

amino acids 1-25

**Putative transmembrane domains:**amino acids 382-398, 402-420, 445-468, 473-491, 519-537, 568-590  
and 634-657**Microbodies C-terminal targeting signal.**

amino acids 691-693

**cAMP- and cGMP-dependent protein kinase phosphorylation sites.**

amino acids 198-201 and 370-373

**N-glycosylation sites.**amino acids 39-42, 148-151, 171-174, 234-237, 303-306, 324-327  
and 341-344**G-protein coupled receptors family 2 proteins**

amino acids 475-504

211/237



**FIGURE 205**

TGCCTGGCCTGCCTTGTCAACAATGCCGCTTACTCTGCTTCCAGGTTGCCCTGCCTTGCAGA  
GGAAANCNTCGGGACTACACCNTCAAGTGCACATGAACCTGCTGCTGGCCGTCTTCCTGCTG  
GACACGAGCTTCCTGCTCAGCGNAGCCGGTGGCCCTGACAGGCTCTGAAGGCTGGCTGCCGA  
GCCAGTGCCATCTTCCTGCACTTCTCCTGCTCACCTGCCTTTCCTGGATGGGCCTCGAGGGG  
TACAACCTCTACCGACTCGTGGTGGAGGTCTTTGGCACCTATGTCCCTGGCTACCTACTCAA  
GCTGAGCGCCATGGGCTGGGGCTTCCCATCTTTCTGGTGACGCTGGTGGCCCTGGTGGATG  
TGGACAACTATGGCCCCATCATCTTGGCTGTGCATAGGACTCCAGAGGGCGTCATCTACCCT  
TCCATGTGCTGGATCCGGGACTCCCTGGTCAGCTACATCACCAACCTGGGCCTCTTCAGCCT  
GGTGTTCCTGTTCAACATGG

## FIGURE 206

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGCTGGTTCAGGTCCA  
GGTTTTGCTTTGATCCTTTTCAAAAACCTGGAGACACAGAAGAGGGCTCTAGGAAAAAGTTTT  
GGATGGGATTATGTGGAACTACCCTGCGATTCTCTGCTGCCAGAGCAGGCTCGGCGCTTCC  
ACCCAGTGCAGCCTTCCCCTGGCGGTGGTGAAAGAGACTCGGGAGTCGCTGCTTCCAAAGT  
GCCC GCCGTGAGTGAGCTCTCACCCAGTCAGCCAAATGAGCCTCTTCGGGCTTCTCCTGCT  
GACATCTGCCCTGGCCGGCCAGAGACAGGGGACTCAGGCGGAATCCAACCTGAGTAGTAAAT  
TCCAGTTTTCCAGCAACAAGGAACAGAACGGAGTACAAGATCCTCAGCATGAGAGAATTATT  
ACTGTGTCTACTAATGGAAGTATTCACAGCCCAAGGTTTCTCATACTTATCCAAGAAATAC  
GGTCTTGGTATGGAGATTAGTAGCAGTAGAGGAAAATGTATGGATACAACCTACGTTTGATG  
AAAGATTTGGGCTTGAAGACCCAGAAGATGACATATGCAAGTATGATTTTGTAGAAGTTGAG  
GAACCCAGTGATGGAACATATATTAGGGCGCTGGTGTGGTTCTGGTACTGTACCAGGAAAACA  
GATTTCTAAAGGAAATCAAATTAGGATAAGATTTGTATCTGATGAATATTTTCTTCTGAAC  
CAGGGTTCTGCATCCACTACAACATTGTCTATGCCACAATTACAGAAAGCTGTGAGTCCTTCA  
GTGCTACCCCTTTCAGCTTTGCCACTGGACCTGCTTAATAATGCTATAACTGCCTTTAGTAC  
CTTGGAAAGACCTTATTCGATATCTTGAACCAGAGAGATGGCAGTTGGACTTAGAAGATCTAT  
ATAGGCCAACTTGGCAACTTCTTGGCAAGGCTTTTGTTTTTTGGAAAGAAAATCCAGAGTGGTG  
GATCTGAACCTTCTAACAGAGGAGGTAAGATTATACAGCTGCACACCTCGTAACTTCTCAGT  
GTCCATAAGGGAAGAACTAAAGAGAACCGATACCATTTTCTGGCCAGGTTGTCTCCTGGTTA  
AACGCTGTGGTGGGAACTGTGCCTGTTGTCTCCACAATTGCAATGAATGTCAATGTGTCCCA  
AGCAAAGTTACTAAAAAATACCACGAGGTCCTTCAGTTGAGACCAAAGACCGGTGTAGGGG  
ATTGCACAAATCACTCACCGACGTGGCCCTGGAGCACCATGAGGAGTGTGACTGTGTGTGCA  
GAGGGAGCACAGGAGGATAGCCGCATCACCACCAGCAGCTCTTGCCAGAGCTGTGCAGTGC  
AGTGGCTGATTCTATTAGAGAACGTATGCGTTATCTCCATCCTTAATCTCAGTTGTTTGCTT  
CAAGGACCTTTTCATCTTCAGGATTTACAGTGCATTCTGAAAGAGGAGACATCAACAGAATT  
AGGAGTTGTGCAACAGCTCTTTTGAGAGGAGGCCATAAGGACAGGAGAAAAGGTCTTCAATC  
GTGGAAAGAAAATTAATGTTGTATTAAATAGTACACCAGCTAGTTTCAGAGTTACCATGTA  
CGTATTCCTAGTCTGGGTTCTGTATTTAGTTCCTTTTCGATACGGCTTAGGGTAATGTCAGT  
ACAGGAAAAAACTGTGCAAGTGAGCACCTGATTCCGTTGCCCTTGCCTAACTCTAAAGCTCC  
ATGTCTGGGCCATAAATCGTATAAATCTGCAATTTTTTTTTTTTTTTTGTCTCATTTTCAC  
ATATGTAAACCAGAACATTCTATGTACTACAAACCTGGTTTTTAAAAAGGAACTATGTTGCT  
ATGAATTAACTTGTGTCTGCTGATAGGACAGACTGGATTTTTTCATATTTCTTATTAATAAT  
TTCTGCCATTTAGAAGAAGAGAACTACATTCATGGTTTGGAAAGAGATAAACCTGAAAAGAAG  
AGTGGCCTTATCTTCACTTTATCGATAAGTCAGTTTATTTGTTTCATTGTGTACATTTTAT  
ATTCTCCTTTTGACATTATAACTGTTGGCTTTTCTAATCTTGTTAAATATATCTATTTTAC  
CAAAGGTATTTAATATTCTTTTTTATGACAACCTAGATCAACTATTTTGTAGCTTGGTAAATT  
TTTCTAAACACAATTGTTATAGCCAGAGGAACAAAGATGATATAAAATATTGTTGCTCTGAC  
AAAAATACATGTATTTTCACTCTCGTATGGTGTAGAGTTAGATTAATCTGCATTTTAAAAAA  
CTGAATTGGAATAGAATTGGTAAGTTGCAAAGACTTTTTGAAAATAATTAAATTATCATATC  
TTCCATTCTGTTATTGGAGATGAAAATAAAAAGCAACTTATGAAAGTAGACATTCAGATCC  
AGCCATTACTAACCTATTCTTTTTTGGGGAAATCTGAGCCTAGCTCAGAAAAACATAAAGC  
ACCTTGAAAAGACTTGGCAGCTTCTGATAAAGCGTGCTGTGCTGTGCAGTAGGAACACAT  
CCTATTTATTGTGATGTTGTGGTTTTTATTATCTTAAACTCTGTTCCATACACTTGTATAAAT  
ACATGGATATTTTATGTACAGAAGTATGTCTCTTAACCAAGTTCACTTATTGTACTCTGGCA  
ATTTAAAAGAAAATCAGTAAAATATTTTGTCTGTAAAATGCTTAATATNGTGCCTAGGTTAT  
GTGGTGACTATTTGAATCAAAAATGTATTGAATCATCAAATAAAAGAATGTGGCTATTTTGG  
GGAGAAAATTAATAAAAAAAAAAAAAAAAAAAGGTTTAGGGATAACAGGGTAATGCGGCC

**FIGURE 207**

MSLFGLLLLT SALAGQRQGTQAESNLSSKFQFSSNKEQNGVQDPQHERIITVSTNGSIHSPR  
FPHTYPRNTVLVWRLVAVEENVWIQLTFDERFGLEDPEDDICKYDFVEVEEPSDGTILGRWC  
GSGTVPGKQISKGNQIRIRFVSDEYFPSEPGFCIHYNIVMPQFTEAVSPSVLPSPALPLDLL  
NNAITAFSTLEDLIRYLEPERWQLDLEDLYRPTWQLLGKAFVFGKRSRVVDLNLLEEVRLY  
SCTPRNFSVSIREELKRTDTIFWPGCLLVKRCGGNCACCLHNCNECQCVPSKVTKKYHEVLQ  
LRPKTGVRGLHKS LTDVALEHHEECDCVCRGSTGG

**FIGURE 208**

CCCATCTCAAGCTGATCTTGGCACCTCTCATGCTCTGCTCTCTTCAACCAGACCTCTACATT  
CCATTTTGGGAAGAAGACTAAAAATGGTGTTCCTAATGTGGACACTGAAGAGACAAATTCTTA  
TCCTTTTTTAACATAATCCTAATTTCCAAACTCCTTGGGGCTAGATGGTTTCTTAAACTCTG  
CCCTGTGATGTCACCTCTGGATGTTCCAAAGAACCATGTGATCGTGGACTGCACAGACAAGCA  
TTTGACAGAAATTCCTGGAGGTATTCCCACGAACACCACGAACCTCACCTCACCATTAAACC  
ACATACCAGACATCTCCCCAGCGTCCTTTACAGACTGGACCATCTGGTAGAGATCGATTTC  
AGATGCAACTGTGTACCTATTCCACTGGGGTCAAAAAACAACATGTGCATCAAGAGGCTGCA  
GATTAAACCCAGAAGCTTTAGTGGACTCACTTATTTAAAATCCCTTTACCTGGATGGAAACC  
AGCTACTAGAGATACCGCAGGGCCTCCCGCTAGCTTACAGCTTCTCAGCCTTGAGGCCAAC  
AACATCTTTTCCATCAGAAAAGAGAATCTAACAGAACTGGCCAACATAGAAATACTCTACCT  
GGGCCAAAACCTGTTATTATCGAAATCCTTGTTATGTTTCATATTCAATAGAGAAAGATGCCT  
TCCTAAACTTGACAAAGTTAAAAGTGCTCTCCCTGAAAGATAACAATGTCACAGCCGTCCTT  
ACTGTTTTGCCATCTACTTTAACAGAACTATATCTCTACAACAACATGATTGCAAAAATCCA  
AGAAGATGATTTTAATAACCTCAACCAATTACAAATCTTGACCTAAGTGGAAATTGCCCTC  
GTTGTTATAATGCCCCATTTCCCTTGTCGCCGCTGTAAAAATAATTCTCCCTACAGATCCCT  
GTAAATGCTTTTGATGCGCTGACAGAATTAAGTTTACGTCTACACAGTAACTCTCTTCA  
GCATGTGCCCCCAAGATGGTTAAGAACATCAACAACTCCAGGAACCTGGATCTGTCCCAAA  
ACTTCTTGCCCAAAGAAATTGGGGATGCTAAATTTCTGCATTTTCTCCCCAGCCTCATCCAA  
TTGGATCTGTCTTCAATTTTGAACCTCAGGTCTATCGTGCATCTATGAATCTATCACAAGC  
ATTTTCTTCACTGAAAAGCCTGAAAATCTGCGGATCAGAGGATATGTCTTTAAAGAGTTGA  
AAAGCTTTAACTCTCGCCATTACATAATCTTCAAAATCTTGAAGTTCTTGATCTTGGCACT  
AACCTTTATAAAAATTGCTAACCTCAGCATGTTTAAACAATTTAAAGACTGAAAGTCATAGA  
TCTTTCAGTGAATAAAATATCACCTTCAGGAGATTCAAGTGAAGTTGGCTTCTGCTCAAATG  
CCAGAACCTTCTGTAGAAAGTTATGAACCCAGGTCTTGGAAACAATTACATTATTTTCAAGAT  
GATAAGTATGCAAGGAGTTGCAGATTCAAAAACAAGAGGCTTCTTTCATGTCTGTTAATGA  
AAGCTGCTACAAGTATGGGCAGACCTTGATCTAAGTAAAATAGTATATTTTTTGTCAAGT  
CCTCTGATTTTTCAGCATCTTCTTTTCTCCTCAATGCTGAATCTGTGAGGAAATCTCATTAGC  
CAAACCTCTTAATGGCAGTGAATTTCAACCTTTAGCAGAGCTGAGATATTTGGACTTCTCAA  
CAACCGGCTTGATTTACTCCATTCAACAGCATTGGAAGAGCTTCAAAAACCTGGAAGTTCTGG  
ATATAAGCAGTAATAGCCATTATTTTCAATCAGAAGGAATTACTCATATGCTAAACTTTACC  
AAGAACCTAAAGGTTCTGCAGAACTGATGATGAACGACAATGACATCTCTTCCCTCCACCAG  
CAGGACCATGGAGAGTGAGTCTCTTAGAACTCTGGAATTCAGAGGAAATCACTTAGATGTTT  
TATGGAGAGAAGGTGATAACAGATACTTACAATTATTCAAGAATCTGCTAAAATAGAGGAA  
TTAGACATCTCTAAAATTTCCCTAAGTTTCTTGCTTCTGGAGTTTTTGTGATGGTATGCCTCC  
AAATCTAAAGAATCTCTCTTTGGCCAAAATGGGCTCAAATCTTTCAGTTGGAAGAACTCC  
AGTGTCTAAAGAACCTGGAACTTTGGACCTCAGCCACAACCACTGACCACTGTCCCTGAG  
AGATTATCCAACCTGTTCCAGAAGCCTCAAGAATCTGATTCTTAAGAATAATCAAAATCAGGAG  
TCTGACGAAGTATTTTCTACAAGATGCCTTCCAGTTGCGATATCTGGATCTCAGCTCAAATA  
AAATCCAGATGATCCAAAAGACCAGCTTCCAGAAAATGTCCTCAACAATCTGAAGATGTTG  
CTTTTGCATCATAATCGGTTTCTGTGCACCTGTGATGCTGTGTGGTTTGTCTGGTGGGTTAA  
CCATACGGAGGTGACTATTCCCTTACCTGGCCACAGATGTGACTTGTGTGGGGCCAGGAGCAC  
ACAAGGGCCAAAGTGTGATCTCCCTGGATCTGTACACCTGTGAGTTAGATCTGACTAACCTG  
ATTCTGTTCTCACTTTCCATATCTGTATCTCTCTTCTCATGGTGATGATGACAGCAAGTCA  
CCTCTATTTCTGGGATGTGTGGTATATTTACCATTTCTGTAAGGCCAAGATAAAGGGGTATC  
AGCGTCTAATATCACCAGACTGTTGCTATGATGCTTTTATTGTGTATGACACTAAAGACCCA  
GCTGTGACCGAGTGGGTTTTGGCTGAGCTGGTGGCCAACTGGAAGACCCAAGAGAGAAACA  
TTTTAATTTATGTCTCGAGGAAAGGGACTGGTTACCAGGGCAGCCAGTTCTGGAAAACCTTT  
CCCAGAGCATACAGCTTAGCAAAAAGACAGTGTGTGTGATGACAGACAAGTATGCAAAGACT  
GAAAATTTTAAGATAGCATTCTTACTTGTCCCATCAGAGGCTCATGGATGAAAAGTTGATGT  
GATTATCTTGATATTTCTTGAGAAGCCCTTTCAGAAGTCCAAGTTCTCCAGCTCCGGAAAA  
GGCTCTGTGGGAGTTCTGTCTTGAGTGGCCAAACAAACCCGCAAGCTCACCCATACTTCTGG  
CAGTGTCTAAAGAACGCCCTGGCCACAGACAATCATGTGGCCTATAGTCAGGTGTTCAAGGA  
AACGGTCTAGCCCTTCTTGCAAAACACAACCTGCCTAGTTTACCAAGGAGAGGCCTGGC

**FIGURE 209**

MVFPMWTLKRQILILFNIILISKLLGARWFPKTLPCDVTLDVDPKNHVIVDCTDKHLTEIPGG  
IPTNTTNLTLTINHIPDISPASFHRLDHLVEIDFRNCNCPVPIPLGSKNNMCIKRLQIKPRSFS  
GLTYLKSLYLDGNQLEIPQGLPPSLQLLSLEANNIFSIRKENLTELANIEILYLGQNCYR  
NPCYVSYSIEKDAFLNLTKLKVLSLKDNNVTAVPTVLPSTLTELYLYNNMIAKIQEDDFNNL  
NQLQILDLSGNCPRCYNAPFPCAPCKNNSPLQIPVNAFDALTELKVRLHLSNSLQHVPPrWF  
KNINKLQELDLSQNFLAKEIGDAKFLHFLPSLIQLDLSFNFELQVYRASMNLSQAFSSLSL  
KILRIRGYVFKELKSFNLSPLHNLQNLVLDLGTNFIKIANLSMFKQFKRLKVIDLSVNKIS  
PSGDSSEVGFCSNARTSVESYEPQVLEQLHYFRYDKYARSCRFKNKEASFMSVNESCYKYGO  
TLDLSKNSIFFVKSSDFQHLSFLKCLNLSGNLISQTLNGSEFQPLAELRYLDFSNNRLDLLH  
STAFEELHKLEVLDISSNSHYFQSEGITMLNFTKNLKVLOKLMMNDNDISSSTSRTMESES  
LRTLEFRGNHLDVLWREGDNRYLQLEFNLLKLEELDISKNSLSFLPSGVFDGMPPNLKNLSL  
AKNGLKFSWKKLQCLKNLETLDLSHNQLTTPPERLSNCSRLKNLILKNNQIRSLTKYFLQ  
DAFQLRYLDLSSNKIQMIQKTSFPENVLNNLKMLLLHHNRFLCTDAVWFVWWVNHTVETIP  
YLATDVTVCVGPAGHKGQSVISLDLYTCELDLTNLILFSLISISVSLFLMVMMTASHLYFWDVW  
YIYHFCKAKIKGYQRLISPCCYDAFIVYDTKDPVTEWVLAELVAKLEDPREKHFNLCLEE  
RDWLPQQPVLENLSQSIQLSKKTVFVMTDKYAKTENFKIAFYLSHQRLMDEKVDVIIILIFLE  
KPFQKSKFLQLRKRLCGSSVLEWPTNPQAHFYFWQCLKNALATDNHVAYSQVFKETV

**FIGURE 210A**

GGGTACCATTCTGCGCTGCTGCAAGTTACGGAATGAAAAATTAGAACAACAGAAAACATGGAA  
AACATGTTCCCTCAGTCGTCAATGCTGACCTGCATTTTCCTGCTAATATCTGGTTCCTGTGA  
GTTATGCGCCGAAGAAAATTTTTCTAGAAGCTATCCTTGTGATGAGAAAAAGCAAAATGACT  
CAGTTATTGCAGAGTGCAGCAATCGTCGACTACAGGAAGTTCCCCAAACGGTGGGCAAATAT  
GTGACAGAACTAGACCTGTCTGATAATTTTCATCACACACATAACGAATGAATCATTTCAAGG  
GCTGCAAAATCTCACTAAAATAAATCTAAACCACAACCCCAATGTACAGCACCAGAACGGAA  
ATCCCGGTATACAATCAAATGGCTTGAATATCACAGACGGGGCATTTCCTCAACCTAAAAAAC  
CTAAGGGAGTTACTGCTTGAAGACAACCAGTTACCCCAAATACCCTCTGGTTTGCCAGAGTC  
TTTGACAGAACTTAGTCTAATTTCAAAACAATATATACAACATAACTAAAGAGGGCATTTCAA  
GACTTATAAACTTGAAAAATCTCTATTTGGCCTGGAACCTGCTATTTTAACAAAGTTTGCGAG  
AAACTAACATAGAAGATGGAGTATTTGAAACGCTGACAAATTTGGAGTTGCTATCACTATC  
TTTCAATTTCTTTTACACGTGCCACCCAAACTGCCAAGCTCCCTACGCAAACCTTTTTCTGA  
GCAACACCCAGATCAAATACATTAGTGAAGAAGATTTCAAGGGATTGATAAATTTAACATTA  
CTAGATTTAAGCGGGAACCTGTCCGAGGTGCTTCAATGCCCATTTCCATGCGTGCCTTGTGA  
TGGTGGTGCCTTCAATTAATATAGATCGTTTTGCTTTTCAAACTTGACCCAACTTCGATACC  
TAAACCTCTCTAGCACTTCCCTCAGGAAGATTAATGCTGCCTGGTTTAAAAATATGCCTCAT  
CTGAAGGTGCTGGATCTTGAATTCAACTATTTAGTGGGAGAAATAGTCTCTGGGGCATTTTT  
AACGATGCTGCCCCGCTTAGAAATACTTGACTTGTCTTTTAACTATATAAAGGGGAGTTATC  
CACAGCATATTAATATTTCCAGAACTTCTCTAAACTTTTGTCTCTACGGGCATTGCATTTA  
AGAGGTTATGTGTTCCAGGAACCTCAGAGAAGATGATTTCCAGCCCCGATGCAGCTTCCAAA  
CTTATCGACTATCAACTTGGGTATTAATTTTATTAAGCAAATCGATTTCAAACCTTTCCAAA  
ATTTCTCCAATCTGGAATTAATTTACTTGTGCAAAAACAGAATATCACCGTTGGTAAAAGAT  
ACCCGGCAGAGTTATGCAAATAGTTCTCTTTTCAACGTCATATCCGGAAACGACGCTCAAC  
AGATTTTGAGTTTGACCCACATTGCAACTTTTATCATTTTACCCGTCCTTTAATAAAGCCAC  
AATGTGCTGCTTATGGAAGCCTTAGATTTAAGCCTCAACAGTATTTTCTTCATTGGGCCA  
AACCAATTTGAAATCTTCTGACATTGCCTGTTTAAATCTGTCTGCAATAGCAATGCTCA  
AGTGTTAAGTGGAACCTGAATTTTCAGCCATTCCTCATGTCAAATATTTGGATTTGACAAACA  
ATAGACTAGACTTTGATAATGCTAGTGCTTACTGAATGTCCGACTTGGAAGTTCTAGAT  
CTCAGCTATAATTCACACTATTTTCAGATAGCAGGCGTAACACATCATCTAATTTATTTCA  
AAATTTTCACAAATCTAAAAGTTTAAACTTGAGCCACAACAACATTTATACTTTAACAGATA  
AGTATAACCTGGAAAGCAAGTCCCTGGTAGAATTAGTTTTTCAAGGTCTCAAGAATCTGACACG  
TTGTGGAATGATGATGACAACAGGTATATCTCCATTTTCAAAGGTCTCAAGAATCTGACACG  
TCTGGATTTATCCCTTAATAGGCTGAAGCACATCCCAAATGAAGCATTCCTTAATTTGCCAG  
CGAGTCTCACTGAACTACATATAAATGATAATATGTTAAAGTTTTTTAACTGGCATTACTC  
CAGCAGTTTCCTCGTCTCGAGTTGCTTGACTTACGTGGAAACAACTACTCTTTTTAACTGA  
TAGCCTATCTGACTTTACATCTTCCCTTCGGACACTGCTGCTGAGTCATAACAGGATTTCC  
ACCTACCTCTGGCTTTCTTTCTGAAGTCAGTAGTCTGAAGCACCTCGATTTAAGTTCCAAT  
CTGCTAAAAACAATCAACAAATCCGCACTTGAACTAAGACCACCACCAAATTATCTATGTT  
GGAACACACGGAAACCCCTTGAATGCACCTGTGACATTGGAGATTTCCGAAGATGGATGG  
ATGAACATCTGAATGTCAAATTTCCAGACTGGTAGATGTCATTTGTGCCAGTCTGGGGAT  
CAAAGAGGGAAGAGTATTGTGAGTCTGGAGCTAACAACCTTGTTTTCAGATGTCACTGCAGT  
GATATTATTTTTCTTCACGTTCTTTATCACCACCATGGTTATGTTGGCTGCCCTGGCTCACC  
ATTTGTTTTACTGGGATGTTTGGTTTTATATATAATGTGTGTTTAGCTAAGGTAAAAGGCTAC  
AGGTCTCTTTCCACATCCCAAACCTTCTATGATGCTTACATTTCTTATGACACCAAAGATGC  
CTCTGTTACTGACTGGGTGATAAATGAGCTGCGCTACCACCTTGAAGAGAGCCGAGACAAAA  
ACGTTCTCCTTTGTCTAGAGGAGAGGGATTGGGACCCGGGATTGGCCATCATCGACAACCTC  
ATGCAGAGCATCAACCAAAGCAAGAAAACAGTATTTGTTTTAACCAAAAAATATGCAAAAAG  
CTGGAACCTTAAAACAGCTTTTTACTTGGCTTTGCAGAGGCTAATGGATGAGAACATGGATG  
TGATTATATTTATCCTGCTGGAGCCAGTGTTACAGCATTCTCAGTATTTGAGGCTACGGCAG  
CGGATCTGTAAGAGCTCCATCCTCCAGTGGCCTGACAACCCGAAGGCAGAAGGCTTGTTTTG  
GCAAACTCTGAGAAATGTGGTCTTGACTGAAAATGATTACGGGTATAACAATATGTATGTCG  
ATTCATTAAGCAATACTAACTGACGTTAAGTCATGATTTTCGCGCCATAATAAAGATGCAAA  
GGAATGACATTTCTGTATTAGTTATCTATTGCTATGTAACAAATTATCCCAAACCTTAGTGG  
TTTAAAACAACACATTTGCTGGCCACAGTTTTTGAGGGTCAGGAGTCCAGGCCAGCATAA

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**FIGURE 210B**

CTGGGTCCTCTGCTCAGGGTGTCTCAGAGGCTGCAATGTAGGTGTTTACCAGAGACATAGGC  
ATCACTGGGGTCACACTCATGTGGTTGTTTTCTGGATTCAATTCCTCCTGGGCTATTGGCCA  
AAGGCTATACTCATGTAAGCCATGCGAGCCTCTCCACAAGGCAGCTTGCTTCATCAGAGCT  
AGCAAAAAAGAGAGGTTGCTAGCAAGATGAAGTCACAATCTTTTGTAATCGAATCAAAAAAG  
TGATATCTCATCACTTTGGCCATATTCTATTTGTTAGAAAGTAAACCACAGGTCCCACCAGCT  
CCATGGGAGTGACCACCTCAGTCCAGGGAAAACAGCTGAAGACCAAGATGGTGAGCTCTGAT  
TGCTTCAGTTGGTCATCAACTATTTCCCTTGACTGCTGTCCTGGGATGGCCTGCTATCTTG  
ATGATAGATTGTGAATATCAGGAGGCAGGGATCACTGTGGACCATCTTAGCAGTTGACCTAA  
CACATCTTCTTTTCAATATCTAAGAACTTTTGCCACTGTGACTAATGGTCCTAATATTAAGC  
TGTTGTTTATATTTATCATATATCTATGGCTACATGGTTATATTATGCTGTGGTTGCGTTTCG  
GTTTTATTTACAGTTGCTTTTACAAATATTTGCTGTAAACATTTGACTTCTAAGGTTTAGATG  
CCATTTAAGAACTGAGATGGATAGCTTTTAAAGCATCTTTTACTTCTTACCATTTTTTAAAA  
GTATGCAGCTAAATTCGAAGCTTTTGGTCTATATTGTTAATTGCCATTGCTGTAAATCTTAA  
AATGAATGAATAAAAATGTTTCATTTTACAAAAA

**FIGURE 211**

MENMFLOQSSMLTCIFLLISGSCELCAEENFSRSPCDEKKQNDSVIAECSNRRLQEVPTVG  
KYVTELDLSDNFITHITNESFQGLQNLTKINLNHNPNVQHONGNPGIQSNGLNITDGAFLNL  
KNLRELLLEDNQLPQIPSGLPESLTELSTLIQNNIYNITKEGISRLINLKNLYLAWNCYFNKV  
CEKTNIEDGVFETLTNLELLSLSFNSLSHVPPKLPSSLRKLELSNTQIKYISEEDFKGLINL  
TLDDLSGNCPRCFNAPFPCVPCDGGASINIDREAFQNLTLRYLNLSSSTSLRKINAAWFKNM  
PHLKVLDLEFNLYLVGEIVSGAFLTMLPRLEILDLSFNYIKGSYPQHINISRNFSKLLSLRAL  
HLRGYVFQELREDDFQPLMQLPNLSTINLGINFIKQIDFKLFQNFSLNLEIYYLSENRIPLV  
KDTRQSYANSSSFQRHIRKRRSTDFFEDPHSNFYHFTRPLIKPQCAAYGKALDLSLNSIFFI  
GPNQFENLPDIACNLNSANSNAQVLSGTEFSAIPHVKYLDLTNNRLDFDNASALTELSDELEV  
LDLSYNSHYFRIAGVTHHLEFIQNFNLKVLNLSHNNIYTLTDKYNLESKSLVELVFSGNRL  
DILWNDDDNRYISIFKGLKNLTRLDLSLNLKHIPNEAFLNLPASLTELHINDNMLKFFNWT  
LLQQFPRLELLDLRGNKLLFLTDSLSDFTSSLRTLLLSHNRISHLPSGFLSEVSSLKHLDL  
SNLLKTINKSALETKTTTKLSMLELHGNPFECTCDIGDFRRWMDEHLNVKIPRLVDVICASP  
GDQRGKSIVSLELTTCVSDVTAVILFFFTFFITTMVLAALAHHLFYWDVWFIYNVCLAKVK  
GYRSLSTSQTIFYDAYISYDTKDASVTDWVINELRYHLEESRDKNVLLCLEERDWDPLAIIID  
NMQSINQSKKTVFVLTCKYAKSWNFKTA FYLALQRLMDENMDVIIIFILLEPVLQHSQYLRL  
RQRICKSSILQWPDNPKAEGLEFWQTLRNVVLTENDSRYNMYVDSIKQY



**FIGURE 212**

CCAGGTCCAACCTGCACCTCGGTTCTATCGATTGAATTCCCCGGGGATCCTCTAGAGATCCCT  
CGACCTCGACCCACGCGTCCGCCAAGCTGGCCCTGCACGGCTGCAAGGGAGGCTCCTGTGGA  
CAGGCCAGGCAGGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCTGAGGCCCCAGC  
AAGGGCTAGGGTCCATCTCCAGTCCCAGGACACAGCAGCGGCCACCATGGCCACGCCTGGGC  
TCCAGCAGCATCAGCAGCCCCCAGGACCGGGGAGGCACAGGTGGCCCCCACCACCCGGAGGA  
GCAGCTCCTGCCCCCTGTCCGGGGGATGACTGATTCTCCTCCGCCAGGCCACCCAGAGGAGAA  
GGCCACCCCGCCTGGAGGCACAGGCCATGAGGGGCTCTCAGGAGGTGCTGCTGATGTGGCTT  
CTGGTGTTGGCAGTGGGCGGCACAGAGCACGCCTACCGGCCCGGCCGTAGGGTGTGTGCTGT  
CCGGGCTCACGGGGACCCTGTCTCCGAGTGGTTCGTGCAGCGTGTGTACCAGCCCTTCTCTCA  
CCACCTGCGACGGGCACCGGGCCTGCAGCACCTACCGAACCATCTATAGGACCGCCTACCGC  
CGCAGCCCTGGGCTGGCCCCCTGCCAGGCCTCGCTACGCGTGCTGCCCCGGCTGGAAGAGGAC  
CAGCGGGCTTCCTGGGGCCTGTGGAGCAGCAATATGCCAGCCGCCATGCCGGAACGGAGGGA  
GCTGTGTCCAGCCTGGCCGCTGCCGCTGCCCTGCAGGATGGCGGGGTGACACTTGCCAGTCA  
GATGTGGATGAATGCAGTGCTAGGAGGGGCGGCTGTCCCCAGCGCTGCATCAACACCGCCGG  
CAGTTACTGGTGCCAGTGTTGGGAGGGGCACAGCCTGTCTGCAGACGGTACACTCTGTGTGC  
CCAAGGGAGGGCCCCCAGGGTGGCCCCCAACCCGACAGGAGTGGACAGTGCAATGAAGGAA  
GAAGTGCAGAGGCTGCAGTCCAGGGTGGACCTGCTGGAGGAGAAGCTGCAGCTGGTGCTGGC  
CCCACTGCACAGCCTGGCCTCGCAGGCACTGGAGCATGGGCTCCCGGACCCCGGCAGCCTCC  
TGGTGCACCTCCTTCCAGCAGCTCGGCCGCATCGACTCCCTGAGCGAGCAGATTTCTTCTCTG  
GAGGAGCAGCTGGGGTCTGTCTCTGCAAGAGAGACTCGTCACTGCCCCAGCSCCCAGGCTG  
GACTGAGCCCCCTCACGCCGCCCTGCAGCCCCCATGCCCTGCCCAACATGCTGGGGGTCCAG  
AAGCCACCTCGGGGTGACTGAGCGGAAGGCCAGGCAGGGCCTTCCTCCTCTTCTCTCTCCCC  
TTCTCGGGAGGCTCCCCAGACCCTGGCATGGGATGGGCTGGGATCTTCTCTGTGAATCCAC  
CCCTGGCTACCCCCACCTGGCTACCCCAACGGCATCCCAAGGCCAGGTGGGCCCTCAGCTG  
AGGGAAGGTACGAGCTCCCTGCTGGAGCCTGGGACCCATGGCACAGGCCAGGCAGCCCGGAG  
GCTGGGTGGGGCCTCAGTGGGGGCTGCTGCCTGACCCCCAGCACAATAAAAAATGAAACGTGA  
AAAGGGCGGCCGCGACTCTAGAGT  
CGACCTGCAGAAGCTTGGCCGCCATGGCCCAACTTGTTTATTGCAGCTTATAATGGTTACAAAT

**FIGURE 213**

MRGSQEVLLMWLLVLAVGGTEHAYRPGRRVCAVRAHGDPVSESFVQRVYQPFLTTCDGHRAC  
STYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNGGSCVQPGRCR  
CPAGWRGDTQCQSDVDECSARRGGCPQRCINTAGSYWCQCWEGHSLSADGTLCVPGGGPPRVA  
PNPTGVDSAMKEEVQRLQSRVDLLEKLQLVLAPLHSLASQALEHGLPDPGSLLVHSFQQLG  
RIDSLSEQISFLEEQLGSCSCKKDS

**FIGURE 214**

GCCAGGCAGGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCTGAGGCCCCAGCAAG  
GGCTAGGGTCCATCTCCAGTCCCAGGACACAGCAGCGGCCACCATGGCCACGCCTGGGCTCC  
AGCAGCATCAGAGCAGCCCCCTGTGGTTGGCAGCAAAGTTCAGCTTGGCTGGGCCCCGCTGTGA  
GGGGCTTCGCGCTACGCCCTGCGGTGTCCCGAGGGCTGAGGTCTCCTCATCTTCTCCCTAGC  
AGTGGATGAGCAACCCAACGGGGGGCCGGGGAGGGGAAGTGGCCCCGAGGGAGAGGAACCCC  
AAAGCCACATCTGTAGCCAGGATGAGCAGTGTGAATCCAGGCAGCCCCCAGGACCGGGGAGG  
CACAGGTGGCCCCCACCACCCGGAGGAGCAGCTCCTGCCCCGTGTCCGGGGGATGACTGATTC  
TCCTCCGCCAGGCCACCCAGAGGAGAAGGCCACCCCGCCTGGAGGCACAGGCCATGAGGGGC  
TCTCAGGAGGTGCTGCTGATGTGGCTTCTGGTGTGGCAGTGGGCGGCACAGAGCACGCCTA  
CCGGCCCCGGCCGTAGGGTGTGTGCTGTCCGGGCTCACGGGGACCCTGTCTCCGAGTCGTTCCG  
TGCAGCGTGTGTACCAGCCCTTCCTCACCACCTGCGACGGGCACCGGGCCTGCAGCACCTAC  
CGAACCATCTATAGGACCGCCTACCGCCGACCCCTGGGCTGGCCCCCTGCCAGGCCTCGCTA  
CGCGTGCTGCCCCGGCTGGAAGAGGACCAGCGGGCTTCCTGGGGCCTGTGGAGCAGCAATAT  
GCCAGCCGCCATGCCGGAACGGAGGGAGCTGTGTCCAGCCTGGCCGCTGCCGCTGCCCTGCA  
GGATGGCGGGGTGACACTTGCCAGTCAGATGTGGATGAATGCAGTGCTAGGAGGGGCGGCTG  
TCCCCAGCGCTGCATCAACACCGCCGGCAGTTACTGGTGCCAGTGTGGGAGGGGCACAGCC  
TGTCTGCAGACGGTACACTCTGTGTGCCAAGGGAGGGCCCCCAGGGTGGCCCCCAACCCG  
ACAGGAGTGGACAGTGCAATGAAGGAAGAAGTGCAGAGGCTGCAGTCCAGGGTGGACCTGCT  
GGAGGAGAAGCTGCAGCTGGTCTGGCCCCACTGCACAGCCTGGCCTCGCAGGCACTGGAGC  
~~ATGGGCTCCCGGACCCCGGCAGCCTCCTGGTGCACTCCTTCCAGCAGCTCCGGCTGCATCGAC~~  
TCCCTGAGCGAGCAGATTTCTTCTGGAGGAGCAGCTGGGGTCCTGCTCCTGCAAGAAAGA  
CTCGTGACTGCCCAGCGCTCCAGGCTGGACTGAGCCCCCTCACGCCGCCCTGCAGCCCCCATG  
CCCCTGCCCAACATGCTGGGGGTCCAGAAGCCACCTCGGGGTGACTGAGCGGAAGGCCAGGC  
AGGGCCTTCCTCCTCTTCCTCCTCCCCCTTCCTCGGGAGGCTCCCCAGACCCTGGCATGGGAT  
GGGCTGGGATCTTCTCTGTGAATCCACCCCTGGCTACCCCCACCCTGGCTACCCCAACGGCA  
TCCCAAGGCCAGGTGGACCCTCAGCTGAGGGAAGGTACGAGCTCCCTGCTGGAGCCTGGGAC  
CCATGGCACAGGCCAGGCAGCCCGGAGGCTGGGTGGGGCCTCAGTGGGGGCTGCTGCCTGAC  
CCCCAGCACATAAAAAATGAAACGTG

**FIGURE 215**

MRGSQEVLLMWLLVLAVGGTEHAYRPGRRVCAVRAHGDPVSESFVQRVYQPFLTTCDGHRAC  
STYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNGGSCVQPGRCR  
CPAGWRGDTQCQSDVDECSARRGGCPQRCINTAGSYWCQCWEGHSLSDGTLCPKGGPPRVA  
PNPTGVDSAMKEEVQRLQSRVDLLEEKQLVLAPLHSLASQALEHGLPDPGSLLVHSFQQLG  
RIDSLSEQISFLEEQLGSCSCKKDS

**FIGURE 216**

CCCACGCGTCCGAAGCTGGCCCTGCACGGCTGCAAGGGAGGCTCCTGTGGACAGGCCAGGCA  
GGTGGGCCTCAGGAGGTGCCTCCAGGCGGCCAGTGGGCCTGAGGCCCCAGCAAGGGCTAGGG  
TCCATCTCCAGTCCCAGGACACAGCAGCGGCCACCATGGCCACGCCTGGGCTCCAGCAGCAT  
CAGCAGCCCCCAGGACCGGGGAGGCACAGGTGGCCCCCACCACCCGGAGGAGCAGCTCCTGC  
CCCTGTCCGGGGGATGACTGATTCTCCTCCGCCAGGCCACCCAGAGGAGAAGGCCACCCCGC  
CTGGAGGCACAGGCCATGAGGGGCTCTCAGGAGGTGCTGCTGATGTGGCTTCTGGTGTGGC  
AGTGGGCGGCACAGAGCACGCCTACCGGCCCCGGCCGTAGGGTGTGTGCTGTCCGGGCTCACG  
GGGACCCCTGTCTCCGAGTCGTTCGTGCAGCGTGTGTACCAGCCCTTCCTCACCACCTGCGAC  
GGGCACCGGGCCTGCAGCACCTACCGAACCATCTATAGGACCGCCTACCGCCGCAGCCCTGG  
GCTGGCCCCCTGCCAGGCCTCGCTACGCGTGCTGCCCCGGCTGGAAGAGGACCAGCGGGCTTC  
CTGGGGCCTGTGGAGCAGCAATATGCCAGCCGCCATGCCGGAACGGAGGGAGCTGTGTCCAG  
CCTGGCCGCTGCCGCTGCCCTGCAGGATGGCGGGGTGACACTTGCCAGTCAGATGTGGATGA  
ATGCAGTGCTAGGAGGGGCGGCTGTCCCCAGCGCTGCGTCAACACCGCCGGCAGTTACTGGT  
GCCAGTGTGTTGGGAGGGGCACAGCCTGTCTGCAGACGGTACACTCTGTGTGCCCAAGGGAGGG  
CCCCCAGGGTGGCCCCCAACCCGACAGGAGTGGACAGTGCAATGAAGGAAGAAGTGCAGAG  
GCTGCAGTCCAGGGTGGACCTGCTGGAGGAGAAGCTGCAGCTGGTGCTGGCCCCACTGCACA  
GCCTGGCCTCGCAGGCACTGGAGCATGGGCTCCCGGACCCCGGCAGCCTCCTGGTGCACTCC  
TTCCAGCAGCTCGGCCGCATCGACTCCCTGAGCGAGCAGATTCCTTCCTGGAGGAGCAGCT  
GGGGTCCTGCTCCTGCAAGAAAGACTCGTGACTGCCCAGCGCCCCAGGCTGGACTGAGCCCT  
TGACGGCCGCTGCAGCCCCCATGCCCTGCCCAACATGCTGGGGGTCCAGAGGCCACCTCG  
GGGTGACTGAGCGGAAGGCCAGGCAGGGCCTTCCTCCTCTTCCTCCTCCCCCTTCCTCGGGAG  
GCTCCCCAGACCCTGGCATGGGATGGGCTGGGATCTTCTCTGTGAATCCACCCCTGGCTACC  
CCCACCCTGGCTACCCCAACGGCATCCCAAGGCCAGGTGGGCCCTCAGCTGAGGGAAGGTAC  
GAGCTCCCTGCTGGAGCCTGGGACCCATGGCACAGGCCAGGCAGCCCGGAGGCTGGGTGGGG  
CCTCAGTGGGGGCTGCTGCCTGACCCCCAGCACATAAAAATGAAACGTG

**FIGURE 217**

MRGSQEVLLMWLLVLAVGGTEHAYRPGRRVCAVRAHGDPVSESFVQRVYQPFLTTCDGHRAC  
STYRTIYRTAYRRSPGLAPARPRYACCPGWKRTSGLPGACGAAICQPPCRNGGSCVQPGRCR  
CPAGWRGDTQCSDVDECSARRGGCPQRCVNTAGSYWCQCWEGHSLSADGTLCVPGGGPPRVA  
PNPTGVDSAMKEEVQRLQSRVDLLEEKQLVLAPLHSLASQALEHGLPDPGSLLVHSFQQLG  
RIDSLSEQISFLEEQLGSCSCKKDS

**FIGURE 218**

GGTTGCCACAGCTGGTTTAGGGCCCCGACCACTGGGGCCCCCTTGTCAGGAGGAGACAGCCTC  
CCGGCCCCGGGGAGGACAAGTCGCTGCCACCTTTGGCTGCCGACGTGATTCCCTGGGACGGTC  
CGTTTTCTGCCGTCAGCTGCCGGCCGAGTTGGGTCTCCGTGTTTCAGGCCGGCTCCCCCTTC  
CTGGTCTCCCTTCTCCCGCTGGGCCGGTTTATCGGGAGGAGATTGTCTTCCAGGGCTAGCAA  
TTGGACTTTTGATGATGTTTGACCCAGCGGCAGGAATAGCAGGCAACGTGATTTCAAAGCTG  
GGCTCAGCCTCTGTTTCTTCTCTCGTGTAATCGCAAACCCATTTTGGAGCAGGAATTCCAA  
TCATGTCTGTGATGGTGGTGAGAAAGAAGGTGACACGGAAATGGGAGAACTCCCAGGCAGG  
AACACCTTTTGCTGTGATGGCCGCGTCATGATGGCCCGGCAAAGGGCATTCTTCTACCTGAC  
CCTTTTCTCATCTCTGGGGACATGTACACTCTTCTTCGCCTTTGAGTGCCGCTACCTGGCTG  
TTCAGCTGTCTCCTGCCATCCCTGTATTGCTGCCATGCTCTTCTTTTCTCCATGGCTACA  
CTGTTGAGGACCAGCTTCAGTGACCCTGGAGTGATTCTCCTGGGCGCTACCAGATGAAGCAGC  
TTTCATAGAAATGGAGATAGAAGCTACCAATGGTGCGGTGCCCCAGGGCCAGCGACCACCGC  
CTCGTATCAAGAATTTCCAGATAAACAACCAGATTGTGAAACTGAAATACTGTTACACATGC  
AAGATCTTCCGGCCTCCCCGGGCCCTCCCATTCAGCATCTGTGACAACTGTGTGGAGCGCTT  
CGACCATCACTGCCCCCTGGGTGGGGAATTGTGTTGGAAAGAGGAACTACCGCTACTTCTACC  
TCTTCATCCTTTTCTCTCTCCCTCCTCACAATCTATGTCTTCGCCTTCAACATCGTCTATGTG  
GCCCTCAAATCTTTGAAAATTGGCTTCTTGGAGACATTGAAAGAACTCCTGGAACGTGTTCT  
AGAAGTCTCATTTGCTTCTTTACACTCTGGTCCGTCTGGGACTGACTGGATTTCATACTT  
TCCTCGTGGCTCTCAACCAGACAACCAATGAAGACATCAAAGGATCATGGACAGGGAAGAAT  
CGCGTCCAGAATCCCTACAGCCATGGCAATATTGTGAAGAACTGCTGTGAAGTGCTGTGTGG  
CCCCTTGCCCCCAGTGTGCTGGATCGAAGGGGTATTTTGCCACTGGAGGAAAGTGGAAGTC  
GACCTCCAGTACTCAAGAGACCAGTAGCAGCCTCTTGCCACAGAGCCCAGCCCCACAGAA  
CACCTGAACTCAAATGAGATGCCGGAGGACAGCAGCACTCCCGAAGAGATGCCACCTCCAGA  
GCCCCAGAGCCACCACAGGAGGCAGCTGAAGCTGAGAAGTAGCCTATCTATGGAAGAGACT  
TTTGTGTTGTGTTAATTAGGGCTATGAGAGATTTAGGTGAGAAGTTAAACCTGAGACAGAG  
AGCAAGTAAGCTGTCCCTTTTAACTGTTTTCTTTGGTCTTTAGTCACCCAGTTGCACACTG  
GCATTTTCTTGCTGCAAGCTTTTTTAAATTTCTGAACTCAAGGCAGTGGCAGAAGATGTCAG  
TCACCTCTGATAACTGGAAAAATGGGTCTCTTGGGCCCTGGCACTGGTTCTCCATGGCCTCA  
GCCACAGGGTCCCCCTTGGACCCCTCTCTTCCCTCCAGATCCACCCCTCTCTGCTTGGCTC  
ACTGGTCTCATTCTGGGGCTAAAAGTTTTTGAGACTGGCTCAAATCCTCCCAAGCTGCTGCA  
CGTGCTGAGTCCAGAGGCAGTCACAGAGACCTCTGGCCAGGGGATCCTAACTGGGTCTTGG  
GGTCTTCAGGACTGAAGAGGAGGGAGAGTGGGGTCAGAAGATTCTCCTGGCCACCAAGTGCC  
AGCATTGCCACAAATCCTTTTAGGAATGGGACAGGTACCTTCCACTTGTTGTANNNNNNNN  
NNNNNNNNNNNNNNNNNNNTGTTTTTCTTTTGAAGTCTGCTCCCATTAGGAGCAGGAATG  
GCAGTAATAAAAGTCTGCACTTTGGTCAATTCTTTTCTCAGAGGAAGCCCGAGTGCTCACT  
TAAACACTATCCCCCTCAGACTCCCTGTGTGAGGCCTGCAGAGGCCCTGAATGCACAAATGGG  
AAACCAAGGCACAGAGAGGCTCTCCTCTCCTCTCCTCTCCCCGATGTACCCTCAAAAAA  
AAAAATGCTAACCAGTTCTTCCATTAAGCCTCGGCTGAGTGAGGGAAAGCCAGCACTGCTG  
CCCTCTCGGGTAACTCACCTAAGGCCTCGGCCACCTCTGGCTATGGTAACCACACTGGGG  
GCTTCTTCCAAGCCCCGCTCTTCCAGCACTTCCACCGGCAGAGTCCAGAGCCACTTCAACC  
TGGGGGTGGGCTGTGGCCCCCAGTCAGCTCTGCTCAGGACCTGCTCTATTTAGGGAAGAAG  
ATTTATGTATTATATGTGGCTATATTTCTAGAGCACCTGTGTTTCTCTTTCTAAGCCAG  
GGTCTGTCTGGATGACTTATGCGGTGGGGGAGTGTAACCGGAACTTTTCTATCTATTTGAA  
GGCGATTAACTGTGTCTAATGCA

**FIGURE 219**

MSVMVVRKKVTRKWEKLPGRNTFCCDGRVMMARQKGI FYLTFLILGTCTLFFAFECRYLAV.  
QLSPAIPVFAAMLFLFSMATLLRTSFSDPGVIPRALPDEAAFIEMEIEATNGAVPQGQRPPP  
RIKNFQINNQIVKLKYCYTCKIFRPPRASHCSICDNCVERFDHHC PWVGNCVGKRNRYFYL  
FILSLSLTIYVFAFNIVYVALKSLKIGFLETLPKTPGTVLEVLI CFFTLWSVVGLTGFHTF  
LVALNQTTNEDIKGSWTGKNRVQNPYSHGNIVKNCCEVL CGPLPPSVLDRRGILPLEESGSR  
PPSTQETSSSLLPQSPAPTEHLNSNEMPEDSSTPEEMPPEPPEPPQEAAEAEK



**FIGURE 220**

AAAACCCTGTATTTTTTACAATGCAAATAGACAATNANCCTGGAGGTCTTTGAATTAGGTAT  
TATAGGGATGGTGGGGTTGATTTTTNTTCCTGGAGGCTTTTGGCTTGGACTCTCNCTTTCT  
CCCACAGAGCNCTTCGACCATCACTGCCCCCTGGGTGGGGAATTGTGTTGGAAAGAGGAACTA  
CCGCTANTTCTACCTCTTCATCCTTTNTCTCTCCNCCTCACAATCTATGTCTTCGCCTTCA  
ACATCGT

**FIGURE 221**

GTTGTGTCCTTCAGCAAAACAGTGGATTTAAATCTCCTTGCACAAGCTTGAGAGCAACACAA  
TCTATCAGGAAAGAAAGAAAGAAAAAACCGAACCTGACAAAAAGAAGAAAAAGAAGA  
AAAAAATCATGAAAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTCAC  
GGGGCTGGCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTTCC  
CCAAAGCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCCTCAGGTGCACTATT  
GACAACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAATGA  
CAAGTGGTGCCTGGATCCTCGCGTGGTCTTCTGAGCAACACCCAAACGCAGTACAGCATCG  
AGATCCAGAACGTGGATGTGTATGACGAGGGCCCTTACACCTGCTCGGTGCAGACAGACAAC  
CACCCAAAGACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCAAAATTGTAGAGATTTT  
TTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACTGGTAGAC  
CAGAGCCTACGGTTACTTGGAGACACATCTCTCCCAAAGCGGTTGGCTTTGTGAGTGAAGAC  
GAATACTTGGAATTCAGGGCATCACCCGGGAGCAGTCAGGGGACTACGAGTGCAGTGCCTC  
CAATGACGTGGCCGCGCCCGTGGTACGGAGAGTAAAGGTCACCGTGAACCTATCCACCATA  
TTTCAGAAGCCAAGGGTACAGGTGTCCCGTGGGACAAAAGGGGACACTGCAGTGTGAAGCC  
TCAGCAGTCCCCTCAGCAGAATTCCAGTGGTACAAGGATGACAAAAGACTGATTGAAGGAAA  
GAAAGGGGTGAAAGTGGAAAACAGACCTTTCCTCTCAAACTCATCTTCTTCAATGTCTCTG  
AACATGACTATGGGAACTACACTTGCGTGGCCTCCAACAAGCTGGGCCACACCAATGCCAGC  
ATCATGCTATTTGGTCCAGGCGCCGTGAGCGAGGTGAGCAACGGCACGTGAGGAGGGCAGG  
CTGCGTCTGGCTGCTGCCTCTTCTGGTCTTGACCTGCTTCTCAAATTTTGATGTGAGTCC  
ACTTCCCCACCCGGGAAAGGCTGCCGCCACCACCACACCAACACACAGCAATGGCAACAC  
CGACAGCAACCAATCAGATATATAACAATGAAATTAGAAGAAACACAGCCTCATGGGACAGA  
AATTTGAGGGAGGGGAACAAAGAATACTTTGGGGGGAAAAGAGTTTTAAAAAAGAAATTGAA  
AATTGCCTTGAGATATTTAGGTACAATGGAGTTTTCTTTTCCCAAACGGGAAGAACACAGC  
ACACCCGGCTTGGAACCACTGCAAGCTGCATCGTGCAACCTCTTTGGTGCCAGTGTGGGCAA  
GGGCTCAGCCTCTCTGCCACAGAGTGCCCCCAGTGGAACATTCTGGAGCTGGCCATCCCA  
AATTCAATCAGTCCATAGAGACGAACAGAATGAGACCTTCCGGCCCAAGCGTGGCGCTGCGG  
GCACTTTGGTAGACTGTGCCACCACGGCGTGTGTTGTGAAACGTGAAATAAAAAGAGCAAAA  
AAAAA

**FIGURE 222**

MKTIQPKMHNSISWAI FTGLAALCLFQGVPRSGDATFPKAMDNVTVRQGESATLRCTIDNR  
VTRVAWLNRSTILYAGNDKWCLDPRVLLSNTQTQYSIEIQNV DVYDEGPYTCSVQTDNHPK  
TSRVHLIVQVSPKIVEISSDISINEGNNISLTCIATGRPEPTVTWRHISPKAVGFVSEDEYL  
EIQGITREQSGDYEC SASNDVAAPVRRVKVTVNYPPYISEAKGTGVPVGQKGT LQCEASAV  
PSAEFQWYKDDKRLIEGKKGVKVENRPFLSKLIFFNVSEHDYGN YTCVASNKLGHTNASIML  
FGPGAVSEVSNGTSRRAGCVWLLPLLVLHLLK F

**FIGURE 223**

GAAAAAAATCATGAAAACCATCCAGCCAAAAATGCACAATTCTATCTCTTGGGCAATCTTC  
ACGGGGCTGGCTGCTCTGTGTCTCTTCCAAGGAGTGCCCGTGCGCAGCGGAGATGCCACCTT  
CCCCAAAGCTATGGACAACGTGACGGTCCGGCAGGGGGAGAGCGCCACCCTCAGGTGCACTA  
TTGACAACCGGGTCACCCGGGTGGCCTGGCTAAACCGCAGCACCATCCTCTATGCTGGGAAT  
GACAAGTGGTGCCTGGATCCTCGCGTGGTCCTTCTGAGCAACACCCAAACGCAGTACAGCAT  
CGAGATCCAGAACGTGGATGTGTATGACGAGGGCCCTTACACCTGCTCGGTGCAGACAGACA  
ACCACCCAAAGACCTCTAGGGTCCACCTCATTGTGCAAGTATCTCCCAAATTGTAGAGATT  
TCTTCAGATATCTCCATTAATGAAGGGAACAATATTAGCCTCACCTGCATAGCAACTGGTAG  
ACCAGAG

**FIGURE 224**

ATGGCTGGTGACGGCGGGGCGGGCAGGGGACCGGGGCGCGGCCGGGAGCGGGCCAGCTG  
CCGGGAGCCCTGAATCACCGCCTGGCCCGACTCCACCATGAACGTCGCGCTGCAGGAGCTGG  
GAGCTGGCAGCAACGTGGGATTCCAGAAGGGGACAAGACAGCTGTTAGGCTCACGCACGCAG  
CTGGAGCTGGTCTTAGCAGGTGCCTCTCTACTGCTGGCTGCACTGCTTCTGGGCTGCCTTGT  
GGCCCTAGGGGTCCAGTACCACAGAGACCCATCCACAGCACCTGCCTTACAGAGGCCTGCA  
TTCGAGTGGCTGGAAAAATCCTGGAGTCCCTGGACCGAGGGGTGAGCCCCTGTGAGGACTTT  
TACCAGTTCTCCTGTGGGGGCTGGATTTCGGAGGAACCCCTGCCCCGATGGGCGTTCTCGCTG  
GAACACCTTCAACAGCCTCTGGGACCAAAACCAGGCCATACTGAAGCACCTGCTTGAAAACA  
CCACCTTCAACTCCAGCAGTGAAGCTGAGCAGAAGACACAGCGCTTCTACCTATCTTGCCTA  
CAGGTGGAGCGCATTGAGGAGCTGGGAGCCCAGCCACTGAGAGACCTCATTGAGAAGATTGG  
TGTTTGGAACATTACGGGGCCCTGGGACCAGGACAACCTTTATGGAGGTGTTGAAGGCAGTAG  
CAGGGACCTACAGGGCCACCCCATCTTCACCGTCTACATCAGTGCCGACTCTAAGAGTTCC  
AACAGCAATGTTATCCAGGTGGACCAGTCTGGGCTCTTTCTGCCCTCTCGGGATTACTACTT  
AAACAGAACTGCCAATGAGAAAGTGCTCACTGCCTATCTGGATTACATGGAGGAACCTGGGGA  
TGCTGCTGGGTGGGCGGGCCACCTCCACGAGGGAGCAGATGCAGCAGGTGCTGGAGTTGGAG  
ATACAGCTGGCCAACATCACAGTGCCCCAGGACCAGCGGCGCGACGAGGAGAAGATCTACCA  
AAGATGAGCAATTCGGAGCTGCAGGCTCTGGCGCCCTCCATGGACTGGCTTGAGTTCTGT  
CTTTCTTGCTGTGCACATTGGAGTTGAGTGACTCTGAGCCTGTGGTGGTGTATGGGATGGAT  
TATTTGCAGCAGGTGTGAGAGCTCATCAACCGCACGGAACCAAGCATCCTGAACAATTACCT  
GATCTGGAACCTGGTGCAAAAGACAACCTCAAGCTGGACCGACGCTTTGAGTCTGCACAAG  
AGAAGCTGCTGGAGACCCTCTATGGCACTAAGAAGTCCGTGTGTGCCGAGGTGGCAGACCTGC  
ATCTCCAACACGGATGACGCCCTTGCGTTTGCTTTGGGGTCACTCTTCGTGAAGGCCACGTT  
TGACCGGCAAAGCAAAGAAATTGCAGAGGGGATGATCAGCGAAATCCGGACCGCATTTGAGG  
AGGCCCTGGGACAGCTGGTTTGGATGGATGAGAAGACCCGCCAGGCAGCCAAGGAGAAGCA  
GATGCCATCTATGATATGATTGGTTTCCCAGACTTTATCCTGGAGCCCAAAGAGCTGGATGA  
TGTTTATGACGGGTACGAAATTTCTGAAGATTCTTTCTTCCAAAACATGTTGAATTTGTACA  
ACTTCTCTGCCAAGGTTATGGCTGACCAGCTCCGCAAGCCTCCCAGCCGAGACCAGTGGAGC  
ATGACCCCCCAGACAGTGAATGCCTACTACCTTCCAACCTAGAATGAGATCGTCTTCCCCGC  
TGGCATCCTGCAGGCCCCCTTCTATGCCCGCAACCACCCCAAGGCCCTGAACCTCGGTGGCA  
TCGGTGTGGTTCATGGGCCATGAGTTGACGCATGCCTTTGATGACCAAGGGCGCGAGTATGAC  
AAAGAAGGGAACCTGCGGCCCTGGTGGCAGAATGAGTCCCTGGCAGCCTTCCGGAACCACAC  
GGCCTGCATGGAGGAACAGTACAATCAATACCAGGTCAATGGGGAGAGGCTCAACGGCCGCC  
AGACGCTGGGGGAGAACATTACTGACAACGGGGGGCTGAAGGCTGCCTACAATGCTTACAAA  
GCATGGCTGAGAAAGCATGGGGAGGAGCAGCAACTGCCAGCCGTGGGGCTCACCAACCACCA  
GCTCTTCTTCGTGGGATTTGCCAGGTGTGGTGTCTCGGTCCGCACACCAGAGAGCTCTCACG  
AGGGGCTGGTGACCGACCCCCACAGCCCTGCCCGCTCCGCGTGTGGGCACTCTCTCCAAC  
TCCCGTGACTTCTGCGGCACTTCGGCTGCCCTGTGGCTCCCCCATGAACCCAGGGCAGCT  
GTGTGAGGTGTGGTAGACCTGGATCAGGGGAGAAATGGCCAGCTGTCACCAGACCTGGGGCA  
GCTCTCTGACAAAGCTGTTTGCTCTTGGGTGGGAGGAAGCAAATGCAAGCTGGGCTGGGT  
CTAGTCCCTCCCCCCCACAGGTGACATGAGTACAGACCTCCTCAATCACCACATTGTGCCT  
CTGCTTTGGGGGTGCCCTGCCCTCAGCAGAGCCCCCACCATTCACTGTGACATCTTCCGT  
GTCACCCTGCCTGGAAGAGGTCTGGGTGGGGAGGCCAGTTCCCATAGGAAGGAGTCTGCC

**FIGURE 225**

MNVALQELGAGSNVGFQKGTRQLLGSRTQLELVLAGASLLLAALLLGCLVALGVQYHRDPSH  
STCLTEACIRVAGKILESIDRGVSPCEDFYQFSCGGWIRRNPLPDGRSRWNTFNSLWDQNQA  
ILKHLENTTFNSSSEAEQKTQRFYLSCLQVERIEELGAQPLRDLEKIGGWNITGPWDQDN  
FMEVLKAVAGTYRATPFFTUYISADSKSSNSNVIQVDQSGFLPSRDYYLNRTANEKVLTA  
LDYMEELGMLLGGRPTSTREOMQQVLELEIQLANITVPQDQRRDEEKIYHKMSISELQALAP  
SMDWLEFLSFLLSPELSDSEPVVVYGM DY LQQVSELINRTEPSILNNYLIWNLVQKTTSSL  
DRRFESAQEKLETLTGKTKSCVPRWQTCISNTDDALGFALGSLFVKATFDRQSKEIAEGMI  
SEIRTA FEEALGQLVWMDEKTRQAAKEKADAIYDMIGFPDFILEPKELDDVYDGYEISEDSF  
FQNMLNLYNFSAKVMADQLRKPPSRDQWSMTPQTVNAYYLPKNEIVFPAGILQAPFYARNH  
PKALNFGGIGVVMGHELTHAFDDQGREYDKEGNLRPWWQNESLA AFRNHTACMEEQYNQYQV  
NGERLNGRQTLGENITDNGGLKAAYNAYKAWLRKHGEEQQLPAVGLTNHQLFFVGFAQVWCS  
VRTPESSHEGLVTDPHSPARFRVLGTLSNSRDFLRHFGCPVGSPMNP GQLCEVW

## FIGURE 226A

GGCCGGCCCTCCGCCCTCCGCACTCCCGCCTCCCTCCCTCCGCCCGCTCCCGGCCCTCCTC  
CCTCCCTCCTCCCCAGCTGTCCCGTTCGCGTCATGCCGAGCCTCCCGGCCCGGCCGCCCCG  
CTGCTGCTCCTCGGGCTGCTGCTGCTCGGCTCCCGGCCGGCCGCGGCGCCGGCCAGAGCC  
CCCCGTGCTGCCATCCGTTCTGAGAAGGAGCCGCTGCCCGTTCGGGGAGCGGCAGGTAGGT  
GGGCGCCCGGGGGAGGCGCGGGCGGGGAGTCGGGCTCGGGGCGAGTCAGCGCCAGCCCGGAG  
GGGCGCGGGGGCGCAGGTGGCTCGGCGCGGGCGGGCGGCCCGGAGGGTGGGCGGGGGCAGAAG  
GGCGCGGTGCCTGGGACCCGGGACCCGCGGGCAGCCCCCGGGCGGCACACGGCGCGAGCTG  
GGCAGCGGCCTCCAGCCAAGCCCGTCCCCGAGGCTGCACCTTCGGCGGGAAGGTCTATGCC  
TTGGACGAGACGTGGCACC CGGACCTAGGGGAGCCATTTCGGGGTGATGCGCTGCGTGCTGTG  
CGCTTGCAGGGCGCAGTGGGGTCGCCGTACCAGGGGCCCTGGCAGGGTCAGCTGCAAGAACA  
TCAAACCAGAGTCCCCAACCCCGGCCTGTGGGCAGCCGCGCCAGCTGCCGGGACACTGCTGC  
CAGACCTGCCCCAGGACTTCGTGGCGCTGCTGACAGGGCCGAGGTGCGAGGCGGTGGCAGG  
AGCCCGAGTCTCGCTGCTGCGCTCTAGCCTCCGCTTCTCTATCTCCTACAGGCGGCTGGACC  
GCCCTACCAGGATCCGCTTCTCAGACTCCAATGGCAGTGTCTGTTTGAGCACCTGCGAGCC  
CCCACCCAAAGATGGCCTGGTCTGTGGGGTGTGGCGGGCAGTGCCTCGGTTGTCTGCGGCT  
CCTTAGGGCAGAACAGCTGCATGTGGCACTTGTGACACTCACTCACCTTCAGGGGAGGTCT  
GGGGGCCTCTCATCCGGCACCGGGCCCTGTCCCCAGAGACCTTCAGTGCCATCCTGACTCTA  
GAAGGCCCCACCAGCAGGGCGTAGGGGGCATCACCTGCTCACTCTCAGTGACACAGAGGA  
CTCCTTGCATTTTTTGCTGCTCTTCCGAGGCGTTGCAGGACTAACCAGGTTCCCTTGAGGC  
TCCAGATTCTACACCAGGGGCAGCTACTGCGAGAATTCAGGCCAATGTCTCAGCCCAGGAA  
CCAGGCTTTGCTGAGGTGCTGCCCAACCTGACAGTCCAGGAGATGGACTGGCTGGTGTGGG  
GGAGCTGCAGATGGCCCTGGAGTGGGCAGGCAGGGCTGCGCATCAGTGGACACATTG  
CTGCCAGGAAGAGCTGCGACGTCTGCAAAGTGTCTTTGTGGGGCTAATGCCCTGATCCCA  
GTCCAAACGGGTGCTGCCGGCTCAGCCAGCCTCACTCTGCTAGGAAATGGCNCCTGATCCT  
CCAGGTGCAATTGGTAGGGACAACCAGTGAGGTGGTGGCCATGACACTGGAAACCAAGCCTC  
AGCGGAGGGATCAGCCCACTGTCTGTGCCACATGGCTGGCCTATCCTCCCTGCCCCAGG  
CCGTGGGTATCTGCCCTGGGCTGGGGTGGCCGAGGGGCTCATATGCTGCTGCAGAATGAGCT  
CTTCTGAACGTGGGCACCAAGGACTTCCCAGACGGAGAGCTTCGGGGGCAACGTGGCTGCC  
CTGCCCTACTCTGGGGCATAGCSCCCGCCCTGCCCGTGCCCTAGCAGGAGCCCTGTCTCTA  
CCCCCTGTGAAGAGCCAAGCAGCAGGGCACGCCTGGCTTTCTTGGATACCCACTGTCACTT  
GCACTATGAAGTGTGCTGGCTGGGCTTGGTGGCTCAGAACAAAGGCACTGTCACTGCCACC  
TCCTTGGGCCTCCTGGAACGCCAGGGCCTCGGCGGCTGCTGAAGGGATTCTATGGCTCAGAG  
GCCCAGGGTGTGGTGAAGGACCTGGAGCCGGAAGTGTGCGGCACCTGGCAAAGGCATGGC  
TTCCCTGATGATCACCACCAAGGTAGCCCCAGAGGGGAGCTCCGAGGGCAGCCTCTCCTCCC  
AGGTGCACATAGCCAACCAATGTGAGGTGGCGGACTGCGCCTGGAGGCGGCCGGGGCCGAG  
GGGGTGGGGCGCTGGGGGCTCCGGATACAGCCTCTGCTGCGCCGCTGTGGTGCCTGGTCT  
CCCGGCCCTAGCGCCCGCCAAACCTGGTGGTCTTGGGCGGGCCCGAGACCCCAACACATGCT  
TCTTCGAGGGGCGCAGCGCCCCACGGGGCTCGCTGGGCGCCCAACTACGACCCGCTCTGC  
TCACTCTGCACCTGCCAGAGACGAACGGTGATCTGTGACCCGGTGGTGTGCCACCGCCAG  
CTGCCACACCCGGTGCAGGCTCCCGACCAGTGTGCCCTGTTGCCCTGGCTGCTATTTTG  
ATGGTGACCGGAGCTGGCGGGCAGCGGGTACGCGGTGGCACCCCGTTGTGCCCCCTTTGGC  
TTAATTAAGTGTGCTGTCTGCACCTGCAAGCAGGGGGGCACTGGAGAGGTGCACTGTGAGAA  
GGTGCAGTGTCCCCGGCTGGCCTGTGCCAGCCTGTGCGTGTCAACCCACCGACTGCTGCA  
AACAGTGTCCAGGTGAGGCCCCACCCCAAGCTGGGGGACCCCATGCAGGCTGATGGGCCCCGG  
GGCTGCCGTTTTGTGTTGGCAGTGGTTCCCAGAGAGTCAGAGCTGGCACCCCTCAGTGCCCC  
GTTTGGAGAGATGAGCTGTATCACCTGCAGATGTGGGGTAAGTGGGGAGCAGAGGCTTGTGT  
GAGGTGGGTACTGGGAGCCTGGTCTGGAGTAGGGAGACCTTCCCAGGGAGGTCCCTGAAGAA  
GCTGAAGGTCACTGTGTCCCAGTGCCTTGGGGGACACTCAGTGTCTGCTGTCTTGTACC  
AGGCAGGGGTGCCCTCACTGTGAGCGGGTACTGTTCACTGCCACTGTCTGTGGCTCGGGG  
AAGGAGAGTCGATGCTGTTCCCGCTGCACGGGCCACCGGCGGCGTAAGTGAGGGAGTCCAGG  
GTCAGCAGCTGTGAGTGGAGGGCTCACCTGCCTGTGGGACTCCTGATCAGGGAAGGGAGCAC  
TCACTGTGTGCAGGAACAGTGCAGCCTGCCACAAAGTGCCATTCCAATCCACCCCTCACAGC  
AACCTGGTGAATGTTATTTATGACCTTTTCTTTACAAATGAGATTCTGAAGCTCAGAGA  
AATTAAGCAACGAGATGAAGGTACCCAGCTGTGTGCACTGACCTGTTTAGAAAATACTGGC

**FIGURE 226B**

CTTTCTGGGACCAAGGCAGGGATGCTTTGCCCTGCCCTCTATGCCTCTCTGTGCCTCTCCAC  
TCCCTCTCCCCTCCTCCAACATTCCCTCCCTTCTGTCTCCAGCAGCCCCAGAGACCAGAAGT  
GATCCAGAGCTGGAGAAAGAAGCCGAAGGCTCTTAGGGAGCAGCCAGAGGGCCAAGTGACCA  
AGAGGATGGGGCCTGAGCTGGGGAAGGGGTGGCATCGAGGACCTTCTTGCATTCTCCTGTGG  
GAAGCCCAGTGCCTTTGCTCCTCTGTCTGCCTCTACTCCCACCCCCACTACCTCTGGGAAC  
CACAGCTCCACAAGGGGGAGAGGCAGCTGGGCCAGACCGAGGTCACAGCCACTCCAAGTCCT  
GCCCTGCCACCCCTCGGCCTCTGTCTGGAAGCCCCACCCCTTTCTTCCTGTACATAATGTCA  
CTGGCTTGTTGGGATTTTTAATTTATCTTCACTCAGCACCAAGGGCCCCGGACACTCCACTC  
CTGCTGCCCCTGAGCTGAGCAGAGTCATTATTGGAGAGTTTTGTATTTATTAAACATTTCT  
TTTTCACTCTTTGGGCATGAGGTTGGCTCTTTGTGGCCAGGAACCTGAGTGGGGCCTGGTGG  
AGAAGGGGCNGAGAGTAGGAGGTGAGAGAGAGGAGCTCTGACACTTGGGGAGCTGAAAGAGA  
CCTGGAGAGGCAGAGGATAGCGTGGC NNTGGCTGGCATNCCTGGGTTCCGCAGAGGGGCTG  
GGGATGGTTCTTGAGATGGTCTAGAGACTCAAGAATTTAGGGAAGTAGAAGCAGGATTTTGA  
CTCAAGTTTAGTTTCCCACATCGCTGGCCTGTTTGCTGACTTCATGTTTGAAGTTGCTCCAG  
AGAGAGAATCAAAGGTGTCACCAGCCCCCTCTCTCCCTCCTTCCCTTCCCTTCCCTTTCTTTC  
CCTCCCCCTCCCCTCCCCTCCCCTCCCCTCC



**FIGURE 227**

GGCCGAGCGGGGGTGCTGCGCGGCGGCCGTGATGGCTGGTGACGGCGGGGCCGGGCAGGGGA  
CCGGGGCCGCGGCCCCGGGAGCGGGCCAGCTGCCGGGAGCCCTGAATCACCGCCTGGCCCCGAC  
TCCACCATGAACGTCGCGCTGCAGGAGCTGGGAGCTGGCAGCAACGTGGGATTCCAGAAGGG  
GACAAGACAGCTGTTAGGCTCACGCACGCAGCTGGAGCTGGTCTTAGCAGGTGCCTCTCTAC  
TGCTGGCTGCACTGCTTCTGGGCTGCCTTGTGGCCCTAGGGGTCCAGTACCACAGAGACCCA  
TCCACAGCACCTGCCTTACAGAGGCCTGCATTCGAGTGGCTGGAAAAATCCTGGAGTCCCT  
GGACCGAGGGGTGAGCCCCCTGTGAGGACTTTTACCAGTTCTCCTGTGGGGGCTGGATTCCGA  
GGAACCCCCCTGCCCCGATGGGCGTTCTCGCTGGAACACCTTCAACAGCCTCTGGGACCAAAAC  
CAGGCCATACTGAAGCACCTGCTTGAAAACACCACCTTCAACTCCAGCAGTGAAGCTGAGCA  
GAAGACACAGCGCTTCTACCTATCTTGCTACAGGTGGAGCGCATTGAGGAGCTGGGAGCCC  
AGCCACTGAGAGACCTCATTGAGAAGATTGGTGGTTGGAACATTACGGGGCCCTGGGACCAG  
GACAACTTTATGGAGGTGTTGAAGGCAGTAGCAGGGACCTACAGGGCCACCCCATTCTTCAC  
CGTCTACATCAGTGCCGACTCTAAGAGTTCCAACAGCAATGTTATCCAGGTGGACCAGTCTG  
GGCTCTTTCTGCCCTCTCGGGATTACTACTTAAACAGAACTGCCAATGAGAAAGTAAGGAAC  
ATCTTCCGAACCCCCATCCCTACCCCTGGCTGAGCTGGGCTGATCCCTGTTGACTTTTCCCT  
TTGCCAAGGGTCAGAGCAGGGAAGGTGAGCCTATCCTGTACCTAGTGAACAACTGCCCTT  
CCTTTCTTTCTTCTTTTCTTCCCTCCCTCCCTTTTCTTCCCCTTTTCTTCCCTTCCCTTCC  
TCTTATTCTTCTAGTAGGTTTTCATAGACACCTACTGTGTGCCAGGTCCAGTGGGGGAATTCCG  
GAGATATAAGTTTCCGAGCCATTGCCACAGGAAGCGTTCACTGTGCGATGGGTTCATGGACCT  
AGATAGCCTGCTTAAACAAAGCTCACAAGAGGGTCTGAGGATTCAGGAGAGACTTATGGAGCC  
AGCAAAGTCTTCCCTGAAGAGATTGCATTTGAGCCAGGTCTGTAG

**FIGURE 228**

ATGCCTACTACCTTCCAATAAGAATGAGATCGTCTTCCCCGCTGGCATCCTGCAGGCCCCC  
TTCTATGCCCCGAACCACCCCAAGGCCCTGAACTTCGGTGGCATCGGTGTGGTCATGGGCCA  
TGAGTTGACGCATGCCTTTGATGACCAAGGGCGCGAGTATGACAAAGAAGGGAACCTGCGGC  
CCTGGTGGCAGAATGAGTCCCTGGCAGCCTTCCGGAACCACACGGCCTGCATGGAGGAACAG  
TACAATCAATACCAGGTCAATGGGGAGAGGCTCAACGGCCGCCAGACGCTGGGGGAGAACAT  
TGCTGACAACGGGGGGCTGAAGGCTGCCTACAATGCTTACAAAGCATGGCTGAGAAAGCATG  
GGGAGGAGCAGCAACTGCCAGCCGTGGGGCTCACCAACCACCAGCTCTTCTTCGTGGGATTT  
GCCCAGGTGTGGTGCTCGGTCCGCACACCAGAGAGCTCTCACGAGGGGCTGGTGACCGACCC  
CCACAGCCCTGCCCCGCTTCCGCGTGCTGGGCACTCTCTCCAACCTCCCGTGACTTCCTGCGGC  
ACTTCGGCTGCCCTGTGCGCTCCCCCATGAACCCAGGGCAGCTGTGTGAGGTGTGGTAGACC  
TGGATCAGGGGAGAAATGGCCAGCTGTCAACAGACCTGGGGCAGCTCTCCTGACAAAGCTGT  
TTGCTCTTGGGTTGGGAGGAAGCAAATGCAAGCTGGGCTGGGTCTAGTCCCTCCCCCCCACA  
GGTGACATGAGTACAGACCCTCCTCAATCACCACATTGTGCCTCTGCTTTGGGGGTGCCCTT  
GCCTCCAGCAGAGCCCCCACCATTCACTGTGACATCTTTCCGTGTACCCCTGCCTGGAAGAG  
GTCTGGGTGGGGAGGCCAGTTCCCATAGGAAGGAGTCTGCCTCTTCTGTCCCCAGGCTCACT  
CAGCCTGGCGGCCATGGGGCCTGCCGTGCCTGCCCCACTGTGACCCACAGGCCTGGGTGGTG  
TACCTCCTGGACTTCTCCCCAGGCTCACTCAGTGCGCACTTAGGGGTGGACTCAGCTCTGTC  
TGGCTCACCTCACGGGCTACCCCCACCTCACCTGTGCTCCTTGTGCCACTGCTCCAGTG  
CTGCTGCTGACCTTCACTGACAGCTCCTAGTGGAAGCCCAAGGGCTCTGAAAGCCTCCTG  
TGGCTCTGTTTCCCTGGGCTGAGAGGGGAGTCCATATGTGTAGCGGTACTGGTTCTGT  
GTCTTAGGGCACAAGCCTTAGCAAATGATTGATTCTCCCTGGACAAAGCAGGAAAGCAGATA  
GAGCAGGGAAAAGGAAGAACAGAGTTTATTTTACAGAAAAGAGGGTGGGAGGGTGTGGTCT  
TGGCCCTTATAGGACC